

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Task Force 5: Expert Testimony and Opinions

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Circulation 2004;110;2535-2537

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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ACCF/AHA Consensus Conference Report

ACCF/AHA Consensus Conference Report on Professionalism and Ethics

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This Conference, sponsored by the American College of Cardiology Foundation and the American Heart Association, was held at Heart House, Bethesda, Maryland, June 2–3, 2004.

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The recommendations set forth in this report are those of the conference participants and do not necessarily reflect the official position of the American College of Cardiology Foundation and the American Heart Association, Inc.

When citing this document, the American College of Cardiology Foundation and the American Heart Association would appreciate the following citation format: ACCF/AHA consensus conference report on professionalism and ethics. Presented in Bethesda, Maryland, June 2–3, 2004. *Circulation*. 2004;110:2506–2549.

This document is available on the World Wide Web sites of the American College of Cardiology (www.acc.org) and the American Heart Association (www.americanheart.org). Single copies of this document as published in the October 19, 2004, issue of the *Journal of the American College of Cardiology* and the October 19, 2004, issue of *Circulation* are available for \$10.00 each by calling 1-800-253-4636 or writing to the American College of Cardiology Foundation, Resource Center, 9111 Old Georgetown Road, Bethesda, MD 20814-1699.

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DOI: 10.1161/01.CIR.0000147952.60985.b0

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INTRODUCTION**Cardiovascular Professionalism and Ethics in the Modern Era**

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The health care professions have always enjoyed special trust and position in our society. Patients trust health care professionals (HCPs) to guard their health, inform them, and put a patient's interests above any other consideration. This is one definition of "professionalism." When HCPs deal with human subjects in research there are basic ethical principles, articulated in the classic Belmont Report of 1979, that have been accepted by all (1).

We believe from our experience that the members and staff of the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) strive to do "good" for society in general and for patients specifically. They put patients' interests first, above their own, in an overwhelming majority of situations. There are virtually hundreds of thousands of patient-HCP encounters daily in the U.S. It is assumed that HCPs are trying their utmost to benefit their patients even when the outcome is not optimal or when disease progression cannot be effectively treated. Complications of therapy occur despite the best of intentions. Clinician-scientists and the medical industry develop new therapies to improve the lives of patients living with cardiovascular disease, and society has seen the benefits of this effort over the past several years. Everything in this system works well until or unless a conflict between the HCP's interests and those of the patient results in actions that harm the patient. Then it is assumed that there has been a breach of that respected patient-HCP trust.

Many modern situations exist in which the personal interest of the HCP may not be aligned with that of the patient. Ethical choices must be made by the HCP in these situations. Examples include:

- A physician is awakened and gets out of bed in the middle of the night to assess a patient with chest pain.
- A procedure is done or an antibiotic is given with marginal indication by the HCP to satisfy the patient's wishes rather than the HCP providing a long or detailed explanation of why the action need not be taken.
- Procedures produce income for HCPs and provide experience and prestige that are valuable for the HCP in ways beyond those only for the individual patient's direct benefit.
- Medical scientists have a deep interest in developing new methods or therapies requiring testing in humans despite the initial imperfection of the agents being tested.

- HCPs continue to devote precious time to help patients make important behavioral changes (smoking and substance abuse cessation, dietary counseling, and so on), despite a lack of reimbursement or support from health care delivery systems and payers.
- An HCP advocates for a product or procedure because of his or her role as an adviser or consultant to a company profiting from the product or procedure while trying to differentiate this role from that of an impartial physician or other HCP educator.
- The HCPs are chosen for their opinions to serve as paid experts in legal actions, de facto taking "sides" in cases related to patient care or product liability issues.
- A physician prescribes a new statin drug for secondary prevention because he or she heard about it at a recent meeting hosted by a drug representative, although this drug is less proven to prevent subsequent events than older medications.

Specific high-profile cases in recent years have brought great attention to the issues of conflict of interest among those dealing with patients and with subjects of clinical trials (2,3). There has been sensationalism in the press addressing some of those cases. In many instances, the important issue centers around the lack of disclosure to all concerned of a potential conflict of interest in the HCP's relationship with the patient. Although these cases are rare, they are very important in our profession.

We must ask ourselves, as members of responsible professional organizations, "what are the issues in modern cardiovascular care that create real or potential problems of conflict of interest for our members and for the organizations themselves?" We believe the first steps toward providing advice and direction for HCPs are to identify such situations and to bring them to an open discussion. We recognize that publication of some of the specific issues addressed in this conference may have the effect of increasing the anxiety of the general public and of the media regarding the extent to which some of the negative situations occur. However, we believe the initial step on the path to setting standards for uniform and optimal behavior for HCPs and the protection of patients is to discuss fully those areas in which we see cause for concern.

The ACCF and the AHA decided to convene this conference in order to highlight the potential conflict of interest in major defined areas and to offer comments about

their management and resolution. We believe it is our responsibility to examine ourselves carefully because the nature of our work and developments in our own specialty of cardiovascular disease allow us to understand the complexities of many of these issues in 2004 perhaps as well as, or better than, others.

This conference, which was held in Bethesda, Maryland, was different from the prior ACCF conferences with "Ethics" in their titles (4,5). With this conference, we have taken a fresh approach since many of the issues to be addressed are "new" in light of the social, economic, and political environment in which we now find ourselves. The participants in the conference were widely experienced and brought both "real-world" and varied perspectives to these issues. They were actively involved in many areas of cardiovascular subspecialty practice, teaching, and research. Some of the cardiovascular specialist participants were employees of industry whose perspectives were seen as important to the discussions. Nevertheless, they were invited as colleagues and not as representatives of industry (nor was their participation sponsored by their companies). Participants did not uniformly agree on every point, but they were able to reach consensus on the issues as expressed in the following Task Force reports.

The Co-Chairs initially did not request a disclosure from attendees regarding their individual relationships with industry as none of the groups addressed or discussed specific companies or products. During the conference and afterward, it was appreciated that having a relationship with

industry might be seen as a factor informing or affecting one's opinion about the general issues discussed and the recommendations made. For this reason, we subsequently asked all participants to disclose such relationships; this disclosure is published as Appendix 1 to these conference reports so those reading the reports may be aware of these relationships with industries.

We believe these reports will be useful for many constituencies. However, the ongoing discussions of the topics covered here are truly the responsibility of the cardiovascular HCPs we represent. A responsible profession must police itself. We hope that this particular function is assisted by this conference. The decision regarding whether to adopt the recommendations from this conference as official policy of the organizations will be the responsibility of the leadership of the ACCF and the AHA.

INTRODUCTION REFERENCES

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TASK FORCES**Task Force 1: The ACCF and AHA
Codes of Conduct in Human Subjects Research***Co-Chairs:* Joseph S. Alpert, MD, FACC, FAHA, Kenneth I. Shine, MD, FACC*Authors:* Robert J. Adams, MD, FAHA, Elliott M. Antman, MD, FACC, FAHA, Rae Ellen W. Kavey, MD, FACC, FAHA*Participants:* Lawrence Friedman, MD, Robert L. Frye, MD, MACC, Robert A. Harrington, MD, FACC, David Korn, MD, Jon F. Merz, JD, PhD, MBA, Elizabeth Ofili, MD, MPH, FACC**SCOPE OF ETHICAL ISSUES
INVOLVED IN HUMAN SUBJECTS RESEARCH**

Human participant research is a crucial element in the development and approval of new drugs, biologics, devices, and procedures that seek to improve patient care. Participation in clinical research is an important professional obligation for cardiovascular practitioners. This involvement ranges from study design and implementation as investigators to the critical role of subject enrollment for all cardiovascular practitioners. The conduct of such research is one of the highest callings of the clinical researcher/practitioner and must be conducted according to the highest standards of science and ethics. All human subjects research should be conducted according to such standards. Difficult issues continue to require awareness and careful management. Some of these issues are examined in this report; conflict of interest is the first of these. A conflict of interest may exist when a secondary interest has the potential to distort, or appear to distort, the integrity of judgment relative to the primary interest. The Hippocratic tradition and the principle of beneficence require that the physician always act in the patient's best interest. However, when the physician profits both professionally and financially from the patient's participation in a clinical trial, the situation may become ethically tenuous for the involved physician. Conversely, information derived from clinical trials improves patient care. Thus, patients may also benefit from participation in clinical trials. This might mitigate, in part, the ethical dilemma just described.

Non-financial conflicts of interest. Physician-investigators obtain a number of non-financial benefits from participation in clinical research trials (1). Career advancement, fulfillment of a desire to do good, an opportunity to publish in a peer-reviewed journal, fame, invitations to present at national and international meetings, future success in obtaining grant funding for research, prestigious research prizes, professional accolades for obtaining a positive outcome from a particular clinical trial, and a personal sense of worth—all potentially accrue to the physician-investigator. Although these non-financial incentives are not well known outside of academia, they are well recognized within the academic community.

Levinsky (2) has recently pointed out that the deaths of three research participants in clinical trials were not related

to financial factors at all. These deaths all occurred at prominent research universities and were apparently the result of excessive zeal, inadequate research, and/or ethical knowledge or training deficits on the part of the investigator and/or his staff (2–5). Financial conflicts of interest are easier for the public to understand. Non-financial conflicts of interest, such as academic promotion and accolades, are often more subtle and may require some thought and study before they become evident. Levinsky (2) suggests that committees charged with the review of experiments involving human subjects (Institutional Review Boards [IRBs]) should consider these non-financial conflicts of interest during their deliberations. Additionally, investigators and those responsible for oversight should be aware of this form of conflict of interest and should bear it constantly in mind during the conduct of a clinical trial.

Clinical trials involving human subjects are essential to the advancement of medical science, but the ethical situation for a physician-investigator who is simultaneously in charge of caring for the patient-subject is particularly challenging. As noted, the physician may benefit in a non-financial manner—for example, from enhanced reputation, publications, and so forth. At the same time, the physician who serves as a clinical investigator enhances his or her own career and may occasionally benefit financially from payments made to the physician or the physician's institution by the sponsor of the clinical trial. Thus, physicians who act as both investigator and attending physician for a patient are caught in a clear ethical dilemma. The physician might subtly coerce or induce the patient to participate in the trial for the physician's personal benefit. This same conflict of interest might also arise in daily clinical practice where the physician profits from the care of the patient (see Task Force 4).

Patients who participate in clinical trials, whether they receive experimental treatment or if they are in a control group, can benefit from meticulous attention to their care, by learning more about their disease process, and potentially, from the trial environment itself (6). Because results of research usually apply more directly to those patient groups included in the studies, it is especially important to include subjects from all socio-economic strata and all ethnic groups. Cardiovascular practitioners should consider

participation of their patients for these reasons, and because this type of research is essential to advance care in the field. The process of enrollment must be undertaken carefully. In addition, a physician must not allow patients to assume, incorrectly, that they will receive the experimental therapy and not the control regimen or device being tested. Physician-investigators may not disabuse their patients' expectations in an overzealous attempt to increase enrollment in the clinical trial. All physician-investigators should bear these points in mind when explaining participation in a clinical trial. This same care should apply to all those recruiting for a clinical trial. These issues become particularly complex in the setting of tertiary care centers, where multiple individuals may be involved in recruiting patients for clinical trials. Indeed, everyone involved in the recruitment process must avoid overzealous recruiting with potential failure to inform the patient adequately concerning the risks involved in the experimental intervention (7–9).

Throughout the clinical trial process, it is important that the physician-investigator maintain a state of mind referred to by ethicists as “equipose.” During the initial discussions with the patient, equipose exists when the physician-investigator accepts the concept of uncertainty about the benefits of one treatment relative to the other. At the analytic stage, equipose exists when the investigator is equally willing to accept a negative or a positive outcome from a clinical trial. Because a positive outcome in a trial is more likely to lead to reward, there is subtle but persistent pressure on the physician-investigator to favor a positive outcome. Such pressure should not lead to multiple re-analyses of trial data in an attempt to state something “positive” about the investigation.

Financial conflicts of interest. Financial relationships are a highly controversial aspect of human research. This topic must be addressed because of the potential for real or perceived conflict of interest. Some physicians devote a substantial portion of their professional life to clinical trial work. For these individuals, a potential problem arises because they derive substantial income from participation in clinical trials. A cardiovascular practitioner may function merely as a “recruiting agent” for large pharmaceutical or device manufacturing companies. This practice is inappropriate and is not condoned as it deviates from the principle of putting a patient’s best interest first. Nevertheless, enrolling patients in clinical trials is critical to advancing cardiovascular care. Participation in trials requires extra time for the cardiovascular practitioner, and this can impact usual patient care flow. Despite these issues, cardiovascular practitioners need to support clinical trial enrollment.

Some physicians are truly the most knowledgeable individuals available with respect to a specific drug or device. It is thus not surprising that industry values the opinion and intellectual assistance of such individuals. It is reasonable for such clinician-investigators to be compensated appropriately for their time and effort. At times, payment includes stock options or even shares in a new company founded to exploit

a new drug or device. In the latter circumstance, the potential financial rewards for the physician-investigator can be substantial. A conflict of interest is clear when such individuals participate in clinical trials of that new drug or device. The physician has a financial stake in the successful initiation, implementation, and outcome stemming from this particular research protocol. At times, such inducements have led physicians to abrogate their social contract with patients, and the results of these ethical failures have occasionally been catastrophic for patients.

Following the passage of the Bayh-Dole Act, academicians were encouraged to transfer their discoveries to industry so the advances could be made available to patients; many academic investigators became integrally involved in the development and testing of innovative biomedical products. The resulting conflicts of interest have attracted the attention of clinical investigators, academic physicians, professional organizations, the media, the federal government, and the public, thereby leading to a number of editorials, surveys, and task force reports dealing with these problems (10–16). The recommendations from all of these commentaries and task force publications are in many ways similar. For example, the threshold employed in most of these documents, including the rules of the National Institute of Health (NIH), defined a “significant” financial arrangement as one that exceeds \$10,000 (see Task Force 3).

THE ROLE OF THE IRB OR HUMAN EXPERIMENTATION REVIEW BOARD IN OVERSEEING RESEARCH INVOLVING HUMAN SUBJECTS

Four comprehensive publications dealing with the regulation of human experimentation have emanated from the Association of American Medical Colleges (AAMC) and the Institute of Medicine within the last three years (13–16). These reports explore the various potential and actual conflicts of interest, financial and non-financial, that exist in human experimentation in the U.S. today. *Responsible Research* describes a systematic approach for improving human subject protection during clinical research trials. A variety of topics are thoroughly examined, including research ethics, the role of the IRB, investigator conflicts of interest, and national and local regulation of human experimentation. Numerous recommendations are presented for improving the current situation. *Preserving Public Trust* is a comprehensive review of the U.S. system of human subject research protection (14). This latter text also suggests numerous reforms for national accreditation and oversight of human subjects review boards (IRBs). Highly prominent in this document is the recommendation that research oversight be expanded to include conflict of interest review by a process independent of the IRB. Two AAMC reports, “Protecting Subjects, Preserving Trust, Promoting Progress I—Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research” (15) and “Protecting Subjects, Preserving Trust, Promoting Progress II—

Principles and Recommendations for Oversight of an Institution's Financial Interests in Human Subjects Research" (16), explore in great detail potential financial conflicts of interest and ways to defend against inappropriate behavioral responses to such conflicts.

THE ACCF/AHA CONSENSUS CONFERENCE RECOMMENDATIONS CONCERNING THE MANAGEMENT OF HUMAN SUBJECT RESEARCH

Physician-Investigator Responsibilities

1. Participation in clinical research is an important obligation for cardiovascular practitioners and is strongly encouraged.
2. Physicians who participate in clinical research must be familiar with both the experimental therapy to be tested and the principles of human subject research.
3. The ACCF/AHA Consensus Conference strongly encourages cardiovascular practitioners to enroll patients who are members of underrepresented groups in clinical trials.

Conflicts of Interest

1. Transparency in all dealings with clinical trial subjects is the cornerstone of management of investigator related conflict of interest. Cardiovascular investigators involved in the clinical trial must disclose their financial conflicts of interest to potential subjects.
2. Investigators must disclose very specific and detailed financial information as per the guidelines in Task Force 3 to the IRB overseeing the trial (13,15).
3. The ACCF/AHA Consensus Conference supports the concept of limitations on the amount of financial involvement that physician-investigators and collaborators may have in a particular research project. Physician-investigators/collaborators with a significant financial relationship (excluding funding for the trial itself) with the sponsor of a particular drug or device under investigation should not personally participate in clinical trials involving these drugs or devices. Unique circumstances can be adjudicated through the IRB mechanism for single-center studies (e.g., primary trial for new drug or device). For multicenter studies, the steering/executive committee for the study should address issues of financial involvement at the individual investigator level. These financial limitations do not apply to employees of the medical product industry.

Informed Consent

1. A trial investigator who is the physician of a potential subject has a special obligation to provide full disclosure of his or her role in the investigation. Because of the vulnerable status of the patient in such circumstances, it must be made clear that refusal to participate in the trial will not affect current or future care.

2. The ACCF/AHA Consensus Conference supports efforts to improve the process of trial enrollment, such as use of a neutral third party (i.e., a research subject advocate or an ombudsman) to observe the informed-consent process and make recommendations for improvement.

IRBs

1. The IRBs should focus on the ethical implications of each and every human research protocol (14). Both financial and non-financial potential conflicts of interest should be addressed.
2. The ACCF/AHA Consensus Conference recommends two separate but coordinated processes, one for the protection of the experimental subjects and one for the examination and management of potential conflicts of interest (financial and non-financial) on the part of the physician-investigator.
3. Investigators should be given ample opportunity to rebut the presumption that they cannot participate in the research due to the conflict of interest that has been raised by the oversight process.
4. Advertising copy aimed at recruiting research subjects should be examined carefully by the IRB to ensure that potentially misleading statements are not included in these ads.
5. Special care must be taken when obtaining informed consent from children and their parents, particularly children too young to comprehend the implications of the suggested intervention. Parental and/or guardian involvement is critical to this process. These same issues apply to other vulnerable individuals including but not limited to the homeless, prisoners, and the uninsured.

Data Analysis, Integrity, and Publication

1. All human subjects' research, not limited to randomized trials, and regardless of sample size, should have a plan for monitoring data collection and subject safety.
2. Physician-investigators should not have a primary role in data analysis of a clinical trial involving a drug or device in which they have a major personal financial interest. This does not apply to employees of the medical products industry (see Task Force 2).
3. At the outset of a sponsored clinical trial involving an experimental therapy, a contractual arrangement should be in place to ensure that publication of the results will not be unduly delayed or obstructed by the sponsor of the trial (see Task Force 2).

WHEN DOES MODIFICATION OF A MEDICAL OR SURGICAL PROCEDURE, DEVICE, OR DRUG BECOME AN EXPERIMENTAL PROCEDURE?

The issue of subtle variations in drugs and devices that have already been approved rising to the level of investigational status is not clearly described in the regulatory literature.

What level of modification is required before an original submission of a new drug or device application is required? Decisions regarding the point of transition from an approved entity to an investigational entity are usually individualized for each product. For the physician who modifies a procedure or a device for use in daily practice, the following distinction is important: "When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is experimental in the sense of new, untested, or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective" (17).

With respect to the development of such new procedures or devices from the point of view of the developer, some guiding principles from the Food and Drug Administration (FDA) document, *Guidance for Industry, Providing Clinical Evidence of Effectiveness for Human Drugs and Biological Products* (May 1998) provide an informative perspective. The purpose of that guidance document was to articulate the FDA's thinking concerning the quantitative and qualitative standards for demonstrating effectiveness of drugs and biologics. The guidance document also describes the evidence necessary to support approval of a new use of an existing drug.

In certain cases, effectiveness of an approved drug or product for a new indication, or effectiveness of a new product, may be adequately demonstrated without additional clinical efficacy trials. Ordinarily, this will be because other types of data provide a way to apply the known effectiveness to a new population or a different dose, regimen, or dosage form. The following are examples of situations in which effectiveness might be extrapolated from efficacy data for another claim or product: bioequivalence, modified-release dosage forms, or different dose regimens.

Single studies for new uses of an existing drug, device, or procedure may be submitted as per the following examples: different doses, regimens, or dosage forms where the relationship between blood concentration and response is less well established; studies in other phases of the disease; studies in other populations; studies in combination or as monotherapy; studies in a closely related disease; studies in a less closely related disease, but where the general purpose of the therapy is similar; studies of different clinical end points; and studies of different pharmacologic/pathophysiologic end points. The Center for Devices and Radiological Health offered an algorithm for submission of evidence for approval of a device (18).

Post-marketing surveillance studies offer the opportunity to submit evidence for a new indication for an existing product. However, in a guidance document on discretionary post-marketing study of pacemaker leads, the FDA has pointed out that the definition of what constitutes a distinct entity versus a minor modification of an existing entity is

highly specific to a particular setting and should be individualized (19).

ISSUES PERTAINING TO HUMAN SUBJECTS RESEARCH INVOLVING SUBJECTS WITH COMPROMISED CAPACITY FOR GIVING INFORMED CONSENT

Within cardiovascular medicine, clinical research may involve individuals with limited capacity to grant informed consent. Although no one contests or argues the critical concept of informed consent, it must be recognized that in the heart/brain injury domains there are several time-sensitive situations in cardiovascular medicine where informed consent may not be practical. These include cardiac resuscitation, brain impairment from stroke, acute myocardial infarction, and severe congestive heart failure. Other vulnerable populations include children and those who are mentally incapacitated. Although research in these populations may be difficult, investigation is particularly important because of limited data to support therapeutic decision-making (20).

Emergency research. Federally sanctioned guidelines allow certain emergency and resuscitation human subjects research to proceed without prospective informed consent (20). The FDA regulations (21 CFR 50.24) provide a narrow exception to the requirement for informed consent from each human subject, or his or her legally authorized representative, before initiation of an experimental intervention. The exception applies to a limited class of research activities involving human subjects who are in need of emergency medical intervention but cannot give informed consent because of their life-threatening medical condition, and/or who do not have a legally authorized person to represent them in a timely fashion. The intent of the regulations is to allow research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent, while establishing additional protections to provide for safe and ethical studies (21 CFR 50.24).

The FDA recognizes that persons with life-threatening conditions who can neither give informed consent nor refuse enrollment are a vulnerable population. Also, the FDA recognizes that the lack of autonomy and inability of subjects to give informed consent requires additional protective procedures in the review, approval, and operation of this research. The exception from the informed-consent requirement permitted by the rule is conditional upon documented findings by an IRB. For this group of patient subjects, a case-by-case independent determination is replaced by the general concurrence of a licensed physician. Readers are referred to the full text of the regulation and the preamble for additional guidance (20).

Research in pediatric patients. Research in pediatric patients (younger than 21 years of age) represents a special challenge because of issues in the informed-consent process,

and because of limitations on the kind of research permitted (21–24). Federal regulations limit clinical research in children to that in which the risks are no greater than minimal; no greater than a minor increase over minimal where the research offers the potential to acquire new knowledge about the child's condition; or where the research offers a prospect for direct benefit to the child. Research that involves greater risk with no prospect of direct benefit to the child may only be performed with permission of the U.S. Secretary of Health and Human Services. Application of the risk and benefit categories is subjective, and, therefore, researchers and IRBs must be careful to ensure that appropriate research is allowed while risk is avoided.

Depending on the level of development, a child may not be competent to provide autonomous consent. Ethically, the best interest of the child must always be considered most important; therefore, one must be more careful to consult with all relevant parties and not use only the standard of autonomy applied in adult consent. For pediatric subjects, what we call "informed consent" is usually a combination of informed parental permission and assent of the child. In this setting, the potential for influence by factors unrelated to the best interest of the child, such as payment for participation, can significantly impact parental decision-making. Therefore, pediatric researchers are particularly obligated to strive for informed consent to the greatest extent possible. For adolescents and young adults, the informed-consent protocol applied to adults should be used (13,15,20,22,24). **Research in cognitively impaired subjects.** Although no specific regulations guiding research in cognitively impaired subjects exist, a comprehensive report was prepared by the National Bioethics Advisory Commission (25). Principles involved in research in this group reflect the vulnerable nature of these populations.

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Task Force 2: Investigator Participation in Clinical Research

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INTRODUCTION

Cardiovascular health care professionals (HCPs) bear a heavy professional responsibility. Indeed, the profession itself is defined by the commitment to place the well-being of the patient ahead of the self-interest of the professional. An obligation of professional behavior of cardiovascular HCPs is to encourage the development of new knowledge that can ultimately improve patient care. One way to accomplish this is by participation in clinical research, which involves a complex interaction of multiple parties (including individuals, institutions, commercial organizations, and regulatory agencies). Because cardiovascular disease is the leading cause of death and disability in the technologically developed world (1) and is projected to increase in prevalence over the next 30 years, appropriate ethical behavior by cardiovascular HCPs could have a major impact on the well-being of both individuals and society. Lack of appropriate participation in efforts to improve care could undermine the delicate balance in the clinical research system (2), which ensures the protection of human subjects and forms the basis for the evidence upon which rational clinical practice is based.

Clinical research studies encompass a broad array of activities, ranging from reviews of medical records to small Phase I safety studies to large multicenter clinical trials. The roles and responsibilities of parties to this complex endeavor have not reached a level of complete clarity. For example, the first textbook on the function of data-monitoring committees was just published in the past two years (3). Accordingly, any effort currently to define appropriate behavior of individual investigators must be viewed as a "moving target."

The most easily identifiable situation in which professional behavior is called into question occurs when the cardiovascular HCP interacts with the industry that invents, manufactures, and sells medical products. The enormous magnitude of the clinical research enterprise and the high financial stakes of transactions between cardiovascular HCPs and the industry provide fertile ground for sensational claims and concerns. Indeed, as technology continues to advance at a rapid pace, the interdependence of cardiovascular HCPs and the medical products industry is increasingly evident. The advances of drugs and devices for

diagnostic and therapeutic purposes have been an overwhelmingly positive development for society, but the large impact of technology on health outcomes and cost reinforces the importance of professional conduct in the development and assessment of these new products.

Although the majority of cardiovascular clinical research is funded by the industry, a significant minority is funded from public sources, most notably the National Heart, Lung, and Blood Institute (NHLBI), a division of the National Institutes of Health (NIH). However, the NHLBI and the NIH as a whole are encouraging public-private partnerships for clinical research (www.nihroadmap.nih.gov), in which resources from both sectors are combined to cover the enormous cost of technology development and evaluation. The principles of appropriate investigator participation are applicable across the range of funding sources, including industry, public sources, and public-private partnerships.

For the most part, the medical products industry and cardiovascular HCPs are aligned in a professional manner. Both aim to develop and use technology that will diagnose cardiovascular disease more accurately, treat it when it is present, and prevent its development in people at risk. However, significant tension and/or conflict of interest may occur in the development and evaluation of medical technology by cardiovascular HCPs. Society rightfully expects that, in evaluating medical products and technology, the cardiovascular HCP will act in a professional manner and place the well-being of patients ahead of his or her personal interests. The industry has given attention to the issue of its interaction with HCPs, and the Advanced Medical Technology Association (AdvaMed) has published a code of ethics on interaction with HCPs that became effective in January 2004 (4).

TYPES OF CONFLICT

Conflict of interest in relation to industry is not a monolithic issue. Rather, there are varying levels of conflict, requiring different remedies to ensure that the public trust is being kept. One consideration is whether the conflict relates to an individual cardiovascular specialist or to an institution as a whole. A second consideration is the intensity of the conflict.

Individual conflict. Conflict of interest may begin with an idea for research, regardless of the source of funding. Those who design clinical trials and observational studies almost always have bias in terms of which theories they favor or upon which they may have staked their professional reputations. Accordingly, when considering the relationship between industry and the profession, one should not dismiss non-financial sources of bias and conflict, but should consider the whole spectrum of conflict. In fact, in general the degree of conflict for an individual may have several aspects as described in the Task Force 1 report and in the following text.

When a physician enrolls patients into clinical studies, a number of individual issues may arise, including questions of financial and personal professional gain. Because research is paid for by a public or private sponsor, the potential financial conflict is obvious to almost everyone involved. Fundamentally, the question is: how can the investigator maintain independence of thought and action from the sponsor in the conduct and evaluation of the research? The endorsement of the concepts involved in a study can lead to bias in how research is conducted and interpreted. However, the major issue in industry-sponsored research, as discussed in the following text, is the relationship between payment and the results of the study. Of equal concern, given the intense pressure on individual HCPs to create a revenue stream through efficient procedure-oriented practice, patients may not be offered the opportunity to participate in clinical research studies because it would reduce the income of the HCP or the practice. This could occur because a revenue-generating procedure might not be performed or because the time spent obtaining consent is compensated at a lower rate than direct clinical activity.

Institutional conflict. Until recently, little attention had been paid to institutional conflict of interest. However, recent difficulties with a particular research project—the Gelsinger case (5)—led to a major report by the Association of American Medical Colleges (AAMC) (6) stressing the difficulties when an institution has equity or other major financial interest in the outcome of a study. When an institution stands to benefit in reputation or finance from a research study, a potential conflict exists. Conversely, an institution can discourage investigation when it interferes with normal operation at the hospital. Additionally, clinical investigators are frequently under intense pressure to generate revenue to support the salaries of research nurses because of lack of reserve funds in institutions and practices to cover those salaries during periods of slow enrollment.

Universities, medical centers, and professional organizations have significant financial entanglements with the industry that go well beyond the conduct of research. The majority of continuing medical education (CME) is funded by industry, and significant donations and funding of training and faculty positions are awarded to academic institutions by industry. Both the American College of Cardiology Foundation (ACCF) and the American Heart

Association (AHA) rely on industry funding in the form of direct support, training money, and exhibits at national meetings (7) (see the Task Force 6 report).

LEVELS OF RESPONSIBILITY AND POTENTIAL CONFLICT

Individual clinicians play a variety of roles in the development and assessment of cardiovascular technology, and these roles may be considered according to the degree to which the clinician is financially involved with the sponsor of the research. At the most basic level, when the industry needs to conduct human research, it must contract with a physician-investigator to perform the research. The investigator, in turn, has a dual responsibility: the primary responsibility is to the research subjects to ensure that the research conforms to the ethical standards defined in documents such as the Declaration of Helsinki (8), the Geneva Declaration (9), and the Belmont Report (10). These obligations are spelled out in the informed-consent document, which is a contract between the investigator and the subject or patient. The second responsibility of the investigator is to complete the research in a professional manner. These issues are detailed in the regulatory document from the Food and Drug Administration entitled “Good Clinical Practices” (11,12). The contract between the investigator and the sponsor provides evidence of the seriousness of this obligation. Therefore, cardiovascular HCPs who enroll patients in clinical research studies have a potential conflict because they are paid to conduct the research, but society has also assigned investigators an independent role to act on behalf of the human subject in the conduct of the research.

A researcher may also be involved in disseminating the research findings. Because most CME is paid for by the medical products industry, interactions with industry are common, both in the writing of manuscripts for the peer-reviewed literature and in the preparation and delivery of lecture materials, slide sets, and other CME materials. Although the dissemination of research findings is increasingly recognized as a responsibility of the clinicians participating in research (13), as discussed in the Task Force 1 report, the degree to which the payment for these activities biases the control of the content of the material represents a potential conflict in this situation, and adherence to standards of conduct in CME is essential (see the Task Force 3 report).

The industry depends heavily on consultants from the academic and practice communities. These consultants offer insight into clinical and scientific issues and often provide feedback on dissemination of ideas and technology into the community. Consultancy contracts can vary considerably, as can the financial transactions around consulting.

A significant number of cardiovascular HCPs become inventors of technology. This privileged position is a major source of societal interest and concern. Much of the advancement of cardiovascular medicine in the U.S. has been

driven by ingenious inventor-investigators who were able to combine scientific and engineering insights with knowledge of cardiovascular medicine (14). A cardiovascular specialist with a patented invention that could result in substantial financial and status benefits and who uses that invention to perform procedures or studies on patients perhaps represents the highest level of direct conflict. It is recognized that the participation of the clinician-inventor in the clinical trial can be valuable. However, the clinician-inventor should not be the principal investigator of the clinical trial. Furthermore, special oversight is necessary when the clinician-inventor is involved in the informed-consent process (15).

Finally, a growing number of cardiovascular HCPs work directly in the medical products industry. This may lead to multiple issues of conflict of interest, particularly in conduct of clinical research developing or evaluating medical products. Such individuals may be involved but should not be the principal investigator of a study.

COMMON ISSUES

Declaration of conflict. When an individual or institution works with the medical products industry, society agrees that disclosure is a minimal standard. Although the issues in CME are discussed in the Task Force 3 report, less energy has been placed on appropriate declarations by investigators enrolling patients in clinical research studies. Recently, the AAMC (6,16,17) guidelines have emphasized disclosure to the patient when the investigator or the institution has equity interest or the potential for royalties in the product being evaluated (6,18). The degree to which these guidelines are being followed has not been quantified. More data needs to be collected in order to evaluate this type of disclosure. At minimum, financial interests must be disclosed to the Institutional Review Board (IRB).

Publication. The conduct of clinical research obligatorily involves an agreement between a subject (often a patient) and an investigator that the study is being done “to create generalizable knowledge.” This term has become standard in the definition of clinical research under which institutional ethics committees review and approve protocols under federal guidelines (18). However, the literature is replete with flaws in the approach to creating this body of knowledge. A critical report by Dickersin (19) highlights the degree to which failure to publish results can lead to inaccurate assessments of the balance of risk and benefit of diagnostic and therapeutic technologies. A particularly interesting report from the Johns Hopkins and Oxford universities (20) documented, in a review of all protocols submitted to institutional IRBs in the 1980s, that industry funding of research is an independent and major predictor of failure to publish. Recent publications have emphasized that this problem has not gone away (21–23), and multiple journals and investigators have called for a registry of all clinical trials (24).

Beyond the failure to publish is the issue of determination

of the editorial content of publications. The content may be heavily influenced by the commercial sponsor in several ways in addition to simply not releasing the data. The sponsor may control the analysis for, or the writing of, the research publication, or may pressure investigators to portray a particular point of view.

A recent trend in the medical products industry is the assignment of publications managers to product development teams. These managers often are company employees, but increasingly major “medical education” firms are combining CME, project promotion, and the production of scientific articles for peer review into package contracts. This effort may lead to “ghost writing,” in which the publications group manager writes the manuscript while the investigators are listed as the authors. This practice seems commonplace in the production of journal supplements, which are highly valuable to industry because the law allows sales representatives to distribute publications from peer-reviewed journals. In this manner, an investigator can write about an off-label use of a product, and although the company cannot advertise that indication, it can distribute the supplement to practitioners. Perhaps of more concern is the use of names of prominent key opinion leaders on major reports from clinical research without independent input or editorial control from these investigators. There should be formal disclosure in the manuscript, if the manuscript is written, in whole or in part, by an individual or group other than the listed authors. All publication supplements should name the sponsor, anyone other than the listed authors involved in preparing the supplement, and whether or not it was peer-reviewed.

An additional issue is access to data. In most industry-funded research, the investigators are restricted from performing their own analyses. The industry sponsor either directly provides statistical support or contracts with a contract research organization for the purpose of analysis for regulatory and publication purposes. The industry contends that access to printouts of the analyses is sufficient to ensure that investigators have independent access to the data (Bayh-Dole Act of 1980; P.L. 96-517). Others have argued that the conduct of the analyses themselves should be in the purview of statisticians and clinicians free of high-level financial ties with the sponsor (25). Finally, the industry can apply significant pressure to investigators who wish to continue to do research with that company to shade reports favorably for the sponsor. The degree to which this happens has not been assessed, although some highly publicized cases have brought the issue to public attention (15,26,27).

These potential problems must be balanced with the legitimate concerns of industry. Many investigators have neither the capacity to manage complex datasets nor the knowledge of biostatistics to do their own analyses. Without the stimulus of industry support, and at times ghost writing, important research results can languish for months to years because of time constraints on academic investigators or lack of motivation and interest. Additionally, unmonitored ac-

cess to data from a study can allow the data to end up in the hands of individuals without either the in-depth knowledge of the topic or the skills to perform appropriate analyses. Optimally, the database should be shared by both the sponsor and the committee responsible for publication (see the following text).

PROPOSED APPROACHES

Accordingly, we advocate the following set of principles to allay the concerns of both cardiovascular specialty investigators and the medical products industry:

- The primary results of human subjects' research must be made public. Surveys or analyses conducted for quality assurance purposes are not intended to be included. When the findings have insufficient priority for publication in the peer-reviewed literature, other means of disseminating knowledge should be used, such as through professional meetings, publicly available archives, web sites, or online tutorials. It is acknowledged that the mechanisms for public disclosure are not yet standardized, but the principle is that the default position in human investigation is that the results of the study should be made public so that they can contribute to generalizable knowledge.
- The publication must adhere to the principles regarding authorship, conflict of interest, and publication ethics as expressed in the International Committee of Medical Journal Editors' "Uniform Requirements" (28).
- A committee responsible for publication should be constituted as part of the contract encompassing multi-site human research studies. All decisions regarding development, authorship, and submission of any manuscript, abstract, or other presentation arising from the study should be made by the committee responsible for publication. Such a committee should be comprised of investigators participating in the study who are scientific and medical experts in their respective fields. It is appropriate to include representatives from the sponsor as full voting members of the committee. The committee responsible for publication should act as an independent body to fulfill the professional obligation to subjects participating in the research by representing their interests and by serving the professional mission of developing, improving, and disseminating scientific and medical knowledge. In small studies, this committee may consist of only a few people involved in the study. In larger studies that could inform clinical practice or better define important mechanisms of disease, such a committee should be carefully constructed as a critical component of the trial's organization.
- The committee responsible for publication should review and approve all analyses and publication topics proposed by participating investigators and institutions, whether based upon the data collected by all participating institutions, by a subset of the participating institutions, or by only a single participating institution.
- The committee responsible for publication should review and constructively critique all proposed submissions that result from an approved analysis or publication topic, and should consider their scientific merit with the aim of promoting the dissemination of scientific and medical knowledge. This should be done in a timely manner before submission for presentation or publication.
- The industry sponsor should ensure that the study data are available for any analysis or publication topic approved by the committee responsible for publication, and the resulting manuscript or presentation should be sent to the sponsor for its timely review and comment. There should be no restrictions on the topics or analytical approaches used in developing manuscripts and presentations. Both the industry sponsor and the investigators should be free to suggest topics and analyses for consideration by the publications committee.
- When the research sponsor chooses to submit publications independent of the committee responsible for publications, the Trial Steering Committee should develop procedures for acknowledgment and disclosure of the publication's relationship to the study.
- In the case of multicenter studies, the first publication of the results of the study should be a multicenter publication reflecting the results of the study as a whole as specified in the protocol and/or statistical analysis plan.
- The author(s) of the initial and subsequent multicenter publication(s), as approved by the committee responsible for publication, should have access to all of the data from the study and should have the ability to analyze those data, independent of the sponsor, although this principle is subject to review of the capability of the authors to perform appropriate analyses. In the case that the investigators are not capable of independent analysis, it is preferable for a statistician independent of the sponsor to be contracted to either perform the analyses or to check the analyses of the sponsor. This statistician should have a copy of the database.
- The initial multicenter publication should be published as soon as practicable after completion of the study, and the committee responsible for publication should attempt to have the first manuscript submitted to a reputable, peer-reviewed biomedical journal within a reasonable period of time (not more than one year) from the end of the study.
- The committee responsible for publication should promptly provide a copy of a planned submission to the Steering Committee for timely review by that committee and the sponsor within a reasonable period of time.
- The committee responsible for publication should review the documents, including any comments from the Steering Committee and sponsor. If confidential information would be released inappropriately in the manuscript or other presentation, it should be removed if possible, or

the sponsor should be given appropriate time to protect intellectual property. However, information that the committee responsible for publication finds to be necessary for the accurate presentation and interpretation of the study results, or which is required by the publishing journal to enable other researchers to reproduce those results, should not be withheld beyond this reasonable period of time (typically 90 days).

- In the conduct of industry-funded clinical research, there is a possibility of the discovery of new findings that could be classified as intellectual property. Typically, the sponsor will desire to claim all intellectual property derived from the research. This stance is understandable given that the industry is paying for the research and requires patent protection to enable the investment in research to recoup profits for its employees and investors. However, after a reasonable period of time has elapsed to protect intellectual property, the intellectual property issue should not be used to limit the publication of results. Although formal review of a manuscript by the sponsor is typically provided in the contract for clinical trials, such review should not unduly delay the dissemination of key trial findings.
- The support of the sponsor must be recognized in any publication or presentation arising from the research or the study. If representatives of the sponsor make substantive contributions to the intellectual content of the manuscript or other presentation, as described in the “Uniform Requirements,” they should be invited to serve as co-authors of the manuscript or other presentation. Acceptance of this invitation should be at the discretion of the representative.

CONFIDENTIALITY

In general, investigators are required to maintain confidentiality with regard to knowledge about the product being evaluated when clinical research is conducted with industry. Given the competitive research environment, this stipulation is quite understandable. Disagreements arise, however, about the scope of confidentiality and the duration of the agreement.

Increasingly, industry has considered confidentiality not only to include intellectual property about the drug or device, but also know-how related to the drug or device and even the protocol itself. This approach has led to extensive delays in the conduct of clinical research because of the requirement to review and sign confidentiality agreements before protocols can be reviewed. Such an approach also inhibits one’s ability to discuss a protocol’s merits and feasibility among professional colleagues. In general, confidentiality about the drug or device seems reasonable, but clinical know-how may belong to the investigator. Protocols should be considered non-confidential at the point at which they are dispersed to principal investigators at the sites, because broad discussion in the clinical community is

required to determine whether the research study is appropriate for the local environment.

Few people in our society are capable of maintaining confidentiality for a lifetime. Accordingly, a time limit is typically placed on the duration of confidentiality. Although there is no objective standard or empirical base on which to make a judgment, confidentiality (except regarding study results—see the following text) should be limited to five years or until the end of the study, whichever is longer.

INDEMNIFICATION

Clinical research is no more immune from our societal preoccupation with lawsuits than is any other area of medicine. Indeed, injury occurring to human subjects has become an increasing source of concern and a topic of increasing interest by the legal profession. In general, the sponsor of the research should hold the investigator harmless for injury complications resulting from conduct of the study in accordance with the protocol. Obviously, the sponsor should not be responsible for negligence in the conduct of the protocol by the investigator.

COMPENSATION

Clinical research is a complex and demanding endeavor. Accordingly, payment for involvement in many aspects of clinical research activities is reasonable and should be expected. The question arises, however, concerning what should constitute reasonable professional standards for payment. Consulting may occur at several points during medical product development and interpretation of data:

- During the early phases of product development, considerable effort is required to guide decision making on the design of the molecule or device and in the design of animal and human studies. As the human studies are conducted, expert advice often is needed for interpretation of the data.
- In the later phases, product acceptance and message acceptance research is commonly done by marketing groups. Individual investigators should be careful to segregate consulting, marketing efforts, and CME into different categories with different purposes (see the Task Force 3 report).
- Conflict can arise at several levels as a result of consulting. When a cardiovascular HCP cares for an individual patient, decisions on product selection are made every day. It is critical to the public trust that neither patient nor product selection be based on payments occurring for the conduct of clinical research.

At a broader level, key opinion leaders can be identified at local, regional, national, and international levels. These individuals are highly valuable to industry because their opinions have a wide impact on prescribing and product-use decisions by other physicians. A complex issue arises when considering payments for lectures and other CME efforts

(see the Task Force 3 report). This becomes particularly important for key opinion leaders who also serve on professional society committees that devise clinical practice guidelines and performance measures (see the Task Force 6 report). The level of compensation should be commensurate with the work performed.

THE INVENTOR-INVESTIGATOR DILEMMA

The investment of the NIH in biomedical research has spawned a large number of investigators who make discoveries that may have beneficial applications to human health. The Bayh-Dole Act (29) instructs academic medical centers to support the transformation of these ideas into commercial reality. Similarly, particularly in the device world, physician entrepreneurs have invented new approaches to technology, leading to "start-up" companies.

Recent events in the arena of gene therapy have highlighted the special nature of this situation. In the highly publicized case of Jesse Gelsinger, a research subject with a genetic deficiency (30), the University of Pennsylvania allegedly had supported the commercialization of an approach to gene therapy delivery. The faculty member was the principal inventor, allegedly with major equity in the commercial entity, and the university also allegedly held major equity. In addition, the experimental material apparently was manufactured at the university. When Jesse, an 18-year-old reasonably healthy boy, died as a direct result of the experimental therapy, the lawyers for the family argued that the process of consent and adverse-event reporting was flawed, and that neither the investigator nor the institution could be unbiased about the human experiment being performed.

Avoiding inventor-investigator conflict of interest. Ideally, invention and investigation of new discoveries should maintain rigorous barriers to avoid both the appearance of and the opportunity for bias (see the Task Force 1 report). Typically, this requires physician-scientists to allow other investigators to perform the human testing of their inventions. Although difficult for some inventors, this approach is the only reliable means to protect both the patient and the scientific integrity of the research. It is often simply too difficult to maintain rigorous standards for evidence-based research for drugs or devices in situations in which an involved inventor stands to profit substantially from the success of the project. Even when the scientific integrity of the investigation is impeccable, other physician-scientists, the public, regulators, and the press are likely to question the independence and reliability of the research. In this situation, fairly strict separation of the inventor is most often the best policy. One exception may occur when the inventor is the best or only person with the skill to operate the device in experimental circumstances involving humans (15,25). In this circumstance, special precautions must be taken to independently verify that subjects are fully informed about the issues involved in their participation. As soon as others

become facile with the device, the inventor-investigator should be removed from experimental subject contact (26).

AVOIDING BIAS IN REPORTING CLINICAL TRIALS

In recent years, disturbing cases have surfaced in which physician-scientists played a passive or active role in publishing scientific results of clinical trials in which it was claimed major distortion of the findings had occurred (26). These issues may involve selective reporting of results in which findings with unfavorable impact on a commercial drug or device were withheld. Such episodes have a devastating effect on the acceptance of clinical trial results, bringing them all under close scrutiny. Several critical principles should govern the analysis and reporting of all clinical trials:

- The physician-investigator should be critically involved in the design of the trial and selection of the efficacy measures.
- A completely passive role, in which the sponsor designs the trial and the physician is "offered" a role as Study Chair or member of the Steering Committee, is unacceptable; such roles may be acceptable if significant input into final study design and conduct occurs.
- The Study Chair and Steering Committee should be signatories to the protocol and to a formal statistical analysis plan (SAP). Studies should be monitored for safety independent of both the sponsor and the investigators (31).
- In reporting results, the investigators should be guided by the SAP and should disclose any analyses that deviate from this plan.
- The editors of the publishing journal should be supplied with the SAP at the time of submission for publication.
- Full disclosure of negative results is imperative. In the case of an entirely negative study, posting on a public web site may be necessary owing to the well-publicized negative reporting bias of medical journals (see the preceding text). When the primary end point of a study is negative but secondary end points seem to be positive, it is critical to emphasize the negative result before discussing the implications of secondary analyses.
- Delay in reporting results that are unfavorable to a drug or device is equally problematic. Such delays may result in reduced quality of care for individual patients, or may lead to another sponsor conducting a similar trial thereby exposing other patients to unneeded risks.

ETHICAL ISSUES IN TRIAL DESIGN: ADEQUATE STATISTICAL POWER

The purpose of the study design should be clear, and it should be able to answer the question being addressed. In this regard, there are appropriate times for pure superiority trials, for non-inferiority trials, and for combined superiority/non-inferiority trials. The key issue is that the

trial design and sample size should be adequate for the stated purpose.

There are conflicting views in the clinical trial community regarding the ethical considerations in deciding the sample size for a trial. Some authorities believe that a deliberately underpowered trial, particularly when the goal of the trial is to demonstrate “non-inferiority,” is inherently unethical. These arguments center on the principle that all trials involve known and unknown risks to the subject. Accordingly, it is appropriate to expose patients to such risks only when the results are likely to provide significant incremental medical knowledge. According to some, an underpowered “non-inferiority” trial cannot benefit medical science, therefore intrinsically constituting an unacceptable risk to the patient. Opponents of this point of view argue that all trials have the potential to result in unanticipated scientific discoveries, and that an underpowered trial may eventually be included in a useful meta-analysis. Accordingly, this problem represents a “gray zone” in clinical trial ethics in which there is no universal agreement. Non-inferiority trials have a place in medicine, but underpowered non-inferiority trials have questionable value.

CONCLUSIONS AND RECOMMENDATIONS

The interaction between cardiovascular HCPs and the medical products industry in the setting of clinical research is complex and evolving. The principles of disclosure are critical. However, continued evaluation, empirical study, and publication of studies examining the “rules of engagement” in clinical research are needed to enable the profession to maintain appropriate independence while participating in a partnership with industry to develop new diagnostic and therapeutic technologies and to assess older ones. Critical principles to be considered by individual investigators are as follows:

- Encouragement for the development of new knowledge is a professional responsibility of cardiovascular HCPs.
- The investigator enrolling patients has an obligation to conduct the study according to the protocol, but also has a legal and ethical responsibility to the human subject from whom consent has been obtained. Thus, although the investigator is obligated to the sponsor he or she has a superseding obligation to act independently from the sponsor if necessary on behalf of the subject.
- Results of human studies must be made public regardless of their outcome. This responsibility can be accomplished preferentially by publication in a peer-reviewed journal, but it may require posting on a public web site or other means of public access.
- In multicenter studies, a formal mechanism for a committee to oversee publication and publish the results should be established by contract before the start of the study. This committee should prevent control of the process either by the sponsor or by individual investigators and should prevent “renegade” publication without due consideration of the interest of the many people who must work together to conduct a clinical research study.
- The complex endeavor of multicenter studies continues to evolve so that standards of conduct and appropriate behavior by all parties will become optimized with continued discussion. Research on methods of performing clinical research and public discussion of the findings of that research should be a high priority for all participants, especially HCPs such as ACCF and AHA members.

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Task Force 3: Disclosure of Relationships With Commercial Interests: Policy for Educational Activities and Publications

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BACKGROUND

Physicians, scientists, patients, and the public rely on professional organizations to provide an independent, unbiased forum for presentation of research, publications, and educational activities at their scientific sessions and in scientific publications. Attendees at educational activities sponsored by not-for-profit organizations usually incur financial and other costs. The attendees expect to gain information from leading experts that may modify their behavior and result in a change in patient care. Concerns about real or perceived conflicts of interest among organizations, physicians, scientists, patients, and educators regarding their relationships with the medical products industry have been debated in the press and in medical journals (1,2). Concerns about these relationships have been discussed extensively by the Association of American Medical Colleges (AAMC), which issued guidelines for conflict of interest in human subjects' research based on a consensus of a committee including clinicians, scientists, legislators, ethicists, consumers, and representatives from commercial interests (3).

The Accreditation Council for Continuing Medical Education (ACCME), which accredits continuing medical education (CME) provider organizations, currently requires full disclosure of pertinent commercial relationships. The ACCME has revised the Standards for Commercial Support which were adopted on April 1, 2004. Both the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) policies must be in compliance to maintain their accreditation (Table 1).

"Disclosure" must never include the use of a trade name or a product-group message. A provider must disclose this information to learners before beginning the educational activity. The ACCME standards allow for relationships to be disclosed verbally, and for a representative of the CME provider who was in attendance to attest in writing that verbal disclosure did occur.

Medical societies have struggled to define a significant financial relationship that poses a real or perceived conflict of interest. The American Society of Clinical Oncology recently amended its regulations to encompass any money exceeding \$100 an investigator received from a firm funding a trial (5). One criticism of this regulation is that the threshold for disclosure is so low that the large number of disclosures might obscure more serious financial relationships. The *New England Journal of Medicine* has maintained that authors of reviews and editorials must not have any financial interest in a company or its competitor that makes a product discussed in the article. Journal editors relaxed the policy for reviewers in June 2002 because their ability to recruit individuals for review articles and editorials was constrained (6). The new policy prohibits a "significant" financial interest, which the journal defined as a lower limit of \$10,000 in accordance with guidelines developed by the National Institutes of Health (7) and the AAMC (3).

The concerns of consumers and professional organizations over conflicts of interest in medical research challenge the ACCF and the AHA to review their policies on conflict of interest, acknowledgment of commercial support, and disclosure of financial relationships with the medical prod-

Table 1. Minimum Requirements for Compliance With ACCME's Standards for Commercial Support: Standards to Ensure the Independence of CME Activities

- CME providers must be able to show that every person in a position to control the content of an educational activity has disclosed all relevant financial relationships with any commercial interest to the provider. The ACCME defines "relevant relationships" as financial relationships in any amount occurring within the past 12 months that create a conflict of interest.
- An individual who refuses to disclose relevant financial relationships will be disqualified from being a planning committee member, a teacher, or an author of CME, and cannot have control of, or responsibility for the development, management, presentation, or evaluation of the CME activity.
- The CME provider must have implemented a mechanism to identify and resolve all conflicts of interest prior to the education activity being delivered to learners. When an individual discloses to learners any relevant financial relationship(s), the information must include:
 - a) The name of the individual
 - b) The name of the commercial interest(s)
 - c) The nature of the relationship the person has with each commercial interest
- The source of all support from commercial interest must be disclosed to learners.
- When commercial support is "in-kind," the nature of the support must also be disclosed to learners.

Source: Excerpt from Accreditation Council for Continuing Medical Education, Standards to Ensure the Independence of CME Activities (4).

ucts industry. The integrity of the ACCF, the AHA, and cardiovascular subspecialty societies as well as their commitment to truth and evidence-based, unbiased scientific inquiry, provides the foundation upon which their missions depend. This fundamental tenet is critical to the validity and success of the various organizations' annual scientific sessions, regional educational meetings, publications, and clinical guidelines.

THE DISCLOSURE POLICY

Introduction. Participants in this Consensus Conference cannot make policy for the ACCF and the AHA. However, we can offer the following for consideration by those organizations with hope they will adopt a uniform policy addressing these issues. The following is meant to demonstrate the ACCF's and AHA's high ethical standards and scientific integrity, and to convey a commitment to ethical behavior.

Policy statement. Audiences for any of the ACCF and the AHA programs, products, policies, services, and scientific publications are to be informed, prior to their participation, of relevant relationships with commercial interests with any proprietary entity producing health care goods or services (with the exception of non-profit or government organizations and non-health care-related companies) on the part of the ACCF and the AHA as organizations and by individual ACCF and AHA contributors (including directors, planners, reviewers, moderators, speakers, faculty, and authors of programs, products, services, and publications). The policy should apply to authors of book chapters and editors of journals. Members of the ACCF and the AHA are expected

to adhere to these policies when they participate in "satellite sessions" around the time of local or national scientific sessions and that are not sponsored or endorsed by the ACCF and the AHA.

These policies also should apply to members who participate in other educational activities such as live case demonstrations, which may serve to disseminate knowledge, management strategies, or advances in technology, but they should not be used primarily to promote a product. The use of the demonstrated technology always should be put in proper clinical perspective. The provision of money by a commercial interest to support a demonstration course must not influence the content of the program.

Finally, it is the current policy of the ACCF and the AHA to comply with the following:

1. The American Medical Association's (AMA) Opinion 8.061, "Gifts to Physicians From Industry" (adopted December 1990) (8) and Opinion 9.011, "Ethical Issues on CME" (adopted by the AMA in December 1993 and updated June 1996) (9).
2. The ACCME's "Standards for Commercial Support" (10).
3. The Accreditation Council for Graduate Medical Education's (ACGME) "Principles to Guide the Relationship Between Graduate Medical Education and Industry" (11).

Individual financial relationships to disclose. The following relevant relationships with commercial interests with any proprietary entity producing health care goods or services (with the exception of non-profit or government organizations and non-health care-related companies) supporting a program, product, service, or document, including financial interest for individual contributors (and his or her spouse and dependent children) or for any foundation or entity controlled or directed by the individual or his or her spouse, must be disclosed before an individual contributor's participation in an ACCF or an AHA activity. The levels recommended in this document were influenced by policies previously established by the National Institutes of Health (7) and by the Food and Drug Administration (12).

The Consensus Conference recommends that relevant relationships be defined in terms of levels and nature of support. The levels are as follows:

- None
- Modest: less than or equal to \$10,000
- Significant: greater than \$10,000

The categories of support are defined as follows:

*Personal Income/Investments**

1. Consulting fees, honoraria (including honoraria from a third party, if the original source is a financially interested company), gifts or other emoluments, or "in kind" compensation from a financially interested company (or entitlement to the same), whether for consulting, lecturing, travel, service on an advisory board,

Table 2. Disclosure of Financial Relationships

Nature of Support	Level of Support	Commercial Entity
Personal Income/Investments	Specify Level	Specify
Royalties/Stock Options	Yes or No	Specify
Programmatic Support	Specify Level	Specify
Cumulative/Total Support	Specify Level	Specify

legal testimony or consultation, or for any other similar purpose in the prior calendar year.

2. Equity interests (or entitlement to the same), including stock options, of any amount in a non-publicly traded and financially related company.
3. Equity interests (or entitlement to the same) in a publicly traded and financially related company (see the exceptions in the following text).
4. Royalty income or the right to receive future royalties under a patent license or copyright, where the topic is directly related to the licensed technology or work under discussion.
5. Any non-royalty payments or entitlements to payments in connection with the activity that are not directly related to the reasonable costs of that activity.
6. Service as an officer, director, or in any other fiduciary role for a financially interested company, whether or not remuneration is received for such service.
7. Sole ownership, partnership, or principal of an enterprise.

*Exceptions: interests of any amount in financially interested company(ies) by virtue of ownership of publicly traded, diversified mutual funds.

Programmatic Support

8. Research grants from a financially interested company.
9. Fellowship support.
10. Funding of a salary or position (partial or full) or "in-kind" support of the program.

A potential conflict of interest level should reflect a cumulative value of personal income/investments and programmatic support. All royalties or stock options should be acknowledged because their value could become significant, and having such arrangements implies a vested interest in the future of the related commercial interest. Full disclosure of relationships with commercial interests should be available to the learner prior to the activity. The speaker must acknowledge whether specific categories and the cumulative value of relationships is none, modest (less than or equal to \$10,000), or significant (greater than \$10,000). The name(s) of the commercial interest(s) must be printed in the syllabus and should be presented verbally or visually on a slide at the time of presentation. The introductory slides should include the information in [Table 2](#).

Both the ACCF and the AHA should develop a uniform secure database, updated yearly, containing full disclosure of relationships with commercial interests for individuals (in-

cluding planners and reviewers of programs and publications) participating in ACCF and AHA educational activities, products, policies, services, and scientific publications.

Disclosure of Financial Relationships to Audiences

The need to disclose specific financial involvement only applies if it is germane to the content of the CME activity or related to commercial supporters of the educational activity. All audiences and readers will be informed, prior to or as an integral part of the activity, whether the contributor: 1) has no individual relationships to disclose as previously described, or 2) has individual relationships to disclose as previously described. It is incumbent on the speaker to provide full disclosure of germane relationships to commercial interests. It is the responsibility of the moderator to request this information at the time of presentation if it has not been provided. Non-compliance, which includes willful refusal or incomplete disclosure, should prohibit future participation by that individual in ACCF and AHA activities.

The ACCF and AHA organizational financial relationships to disclose should be acknowledged before or as an integral part of the activity by indicating the corporate name of the supporter and the level of financial support as previously defined.

MECHANISMS FOR DISCLOSURE

Participants in educational activities. The content or format of a CME activity or its related materials must promote improvements or quality in health care and not specific proprietary business or commercial interests. Presentations must offer a balanced view of therapeutic options. Use of generic names will contribute to impartiality. If the CME educational material or content includes trade names, where available, trade names of products from several companies should be used, not just trade names from a single company. The program syllabus and/or a slide should disclose relationships with commercial interests to identify a potential conflict of interest of both planners and reviewers.

Authors of editorials and original articles. The ACCF and AHA journal editors should obtain information regarding relationships with industry at the time of submission of an original manuscript and before inviting an editorial submission from an expert. When feasible, an additional expert opinion may be sought from another peer without a potential conflict of interest. Transparency concerning potential conflict of interest for authors of original publications and editorialists is sufficiently important to warrant a more in-depth statement specifying the nature and magnitude of the relevant relationship with a commercial entity. The information disclosed should include: 1) the name of the individual, 2) the name of the company/enterprise, 3) the nature of the contract with industry (e.g., data handling, statistics, censorship of results, ability to report adverse findings), and 4) the level of financial support.

Members of the writing groups of the ACCF and the AHA scientific statements and practice guidelines. The potential conflict of interest of the writing group should be provided in detail. The ACC/AHA Task Force on Practice Guidelines developed a policy for the guideline process that incorporates several unique elements (8). The Consensus Conference endorses this approach. Each writing committee member is required to make full oral disclosure at the initial writing committee meeting of any potential conflict of interest. At each subsequent meeting, a written summary of disclosure is provided to the entire committee, and each member is asked to update his or her information regarding any new potential conflict of interest. Full disclosure is thought to be critical to the credibility of the process, and it is carefully monitored by the Task Force. Those members of the writing committee who have disclosed a relationship with industry are invited to supply information on the topic for which they provided a disclosed relationship, but they are excused from the room for the vote on guideline recommendations pertaining to the disclosed conflict. Information on relationships with commercial interests for each writing group member and peer reviewer of a practice guideline is published with the document. Finally, members of the writing committee are prohibited from sharing information pertinent to the writing effort with commercial interests until the document has been posted on the ACC and/or AHA web sites.

CONSEQUENCES FOR NONCOMPLIANCE

Personal and professional. Consequences for refusal or failure to disclose a relationship with industry or to be willfully out of compliance with the ACCF and the AHA policies need to be substantial enough to ensure the integrity of the policies. The policies and potential sanctions should be fully disclosed to all participants in educational activities, products and services, and publications. The ACC/ACCF Ethics and Discipline Committee and the AHA Conflict of Interest Review Committee should be responsible for administering and enforcing appropriate sanctions. The ACCF and the AHA should create a mechanism to randomly audit disclosures and to create a process where ACCF and AHA members and attendees of educational activities can report potential violations, including partial disclosure or non-disclosure, for further investigation.

Refusal by an individual to provide adequate disclosure consistent with the conflict of interest policy should prohibit participation by that individual in ACCF and AHA activities. As a further safeguard, violations may also be reported to the individual's academic institution or entity with whom he or she is professionally affiliated.

A mechanism should be established for disqualification of individuals with a conflict of interest that cannot be adequately dispelled with disclosure. Such matters might be placed under the jurisdiction of the ACC/ACCF Ethics

and Discipline Committee and the AHA Conflict of Interest Review Committee.

Potential legal risks. The Office of the Inspector General of the U.S. Department of Health and Human Services (HHS) has published a Compliance Program Guidance (13) relevant to this subject. Because HHS is responsible for proper use of Medicare and other government programs, it is vigilant to prevent improper use of the program funds. The Guidance speaks to support provided by pharmaceutical manufacturers in Section B: "Key Areas of Potential Risk." With regard to educational grants, the Guidance addresses the issue that, to the extent the medical product manufacturer has any influence over the substance of an educational program or the speaker, there is a risk that the educational program may be used for inappropriate marketing purposes.

To reduce the risks that a program supported by a grant is used improperly to induce or reward product purchases or to market products inappropriately, manufacturers are advised to separate their grant-making function from the sales and marketing function. Effective separation of these functions should help ensure that grant funding is not inappropriately influenced by sales or marketing motivations and that the educational purposes of the grant are legitimate. With regard to research funding, the Guidance advises clear separation of research contracts from marketing.

The HHS Guidance also states that manufacturers, providers, and suppliers of health care products and services frequently cultivate relationships with physicians in a position to generate business for them through a variety of practices, including gifts, entertainment, and personal services compensation arrangements. The activities have a potential for fraud and abuse and, historically, have generated a substantial number of anti-kickback convictions (see the Task Force 4 report). The Guidance speaks to consulting and advisory payments and conveys concern about compensation relationships with physicians for services connected directly or indirectly to a manufacturer's marketing sales activities, such as speaking, certain research, or preceptor or "shadowing" services. These may pose a risk of fraud and abuse. It is important to note that the Guidance is advisory in intent; nonetheless, it does have the legal authority of federal anti-kickback statute, which poses risk of prosecution by the U.S. Attorney General's office.

RECOMMENDATIONS

The Consensus Conference believes the policies proposed herein would represent the ACCF, the AHA, and cardiovascular subspecialty societies' commitment and dedication to the highest levels of professionalism and ethical behavior in educational activities and publications. Therefore, the Consensus Conference proposes the following recommendations:

1. Disclosure of financial relationships with commercial interests should be mandatory for educational activities and publications (original articles, policy statements, editorials, texts, and guidelines). The policy and disclosure guidance

discussed in this document should be adopted by the ACCF, the AHA, and cardiovascular subspecialty societies using as uniform a mechanism as possible.

2. The ACCF, the AHA, and cardiovascular subspecialty societies should develop a secure uniform database containing full disclosure of relationships with commercial interests for individuals (including planners and reviewers of programs and publications) participating in ACCF and AHA educational activities, products, policies, services, and scientific publications. The database should be updated yearly.
3. The ACCF, the AHA, and cardiovascular subspecialty societies should educate their members and promote compliance with: the AMA's policy on "Gifts to Physicians from Industry" (8); the ACCME's "Standards for Commercial Support" (10); and the ACGME's "Principles to Guide the Relationship Between Graduate Medical Education and Industry" (11).

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Task Force 4: Appropriate Clinical Care and Issues of "Self-Referral"

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INTRODUCTION

"Professionalism is the basis of medicine's contract with society. It demands placing the interests of patients above those of the physician, setting and maintaining standards of competence and integrity, and providing expert advice to society on matters of health . . . Essential to this contract is public trust in physicians, which depends on the integrity of both individual physicians and the whole profession" (1). Cardiovascular specialists support the fundamental principles of primacy of patient welfare, patient autonomy, and the promotion of social justice.

For the purposes of this document, "self-referral" occurs when a physician recommends a patient intervention from which the physician may benefit personally. Such recommendations usually facilitate the provision of efficient, effective, and high-quality care, but may also afford the potential for abuse. As former *JACC* Editor-in-Chief

William Parmley stated so clearly: "At issue is the question of intent; if the intent is to provide excellent medical care, the practice is laudable. If the intent is to subjugate medical decision-making, then the practice is unethical" (2). Those few physicians who are publicized for violating our trust do not reflect the rank and file of cardiovascular specialists.

The cardiovascular specialist's primary duty is to the patient. His or her role is to promote patient welfare in an increasingly complex health care environment, one that has been made even more complex by the anti-kickback statutes and Stark laws (see the following sections). Having entered into a physician-patient relationship, physicians must counsel their patients regardless of individual financial or medical care delivery system considerations or other factors, such as socio-economic status, race, gender, or sexual orientation (3). The physician's clinical judgment must not be influenced by financial incentives from a fee-for-service system

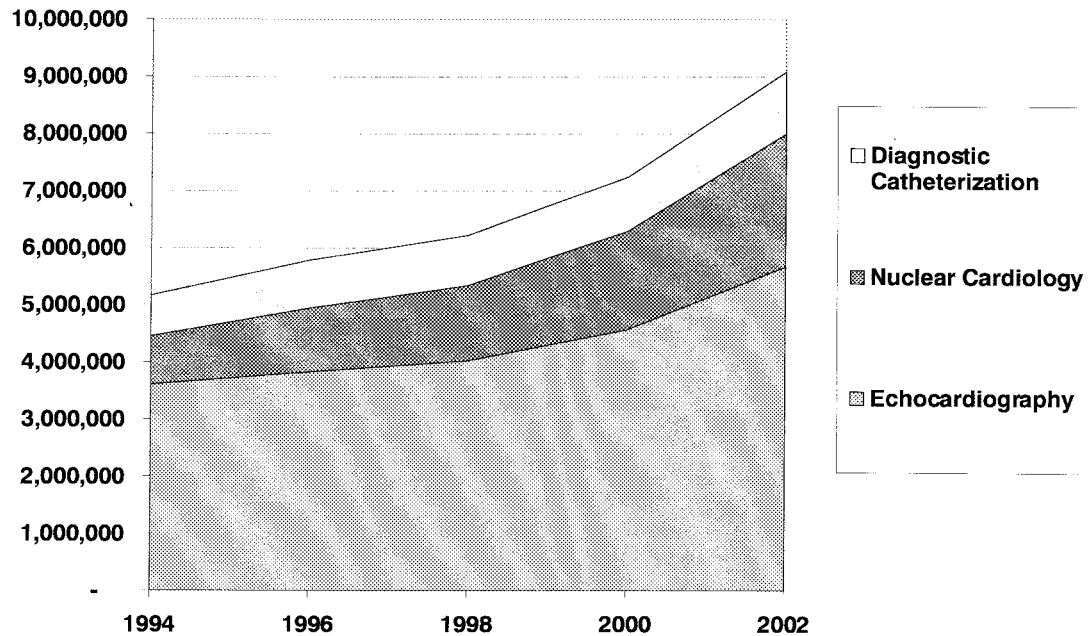


Figure 1. Number of cardiovascular imaging procedures among Medicare patients, 1994 to 2002.

or disincentives from a capitated care system. Recommendations should be made based only on medical merit (4,5). Physicians must also contribute to the responsible stewardship of health care resources.

Growth and geographic variation in cardiac procedures.

The use of cardiac procedures in the U.S. is increasing over time. Figure 1 displays changes in the number of diagnostic cardiac procedures performed for Medicare patients between 1994 and 2002. Office-based procedures account for much of the rise in nuclear and echocardiographic testing. Many factors, such as the aging of the population, the epidemic of diabetes and obesity, advances in technology, and new therapies, may partially drive these increases. Studies have demonstrated marked geographic variations in the use of both invasive and non-invasive cardiac procedures (6–10). The exact cause for geographic variation in procedure use remains elusive. Similar studies have found a linear relationship between the availability of cardiovascular diagnostic equipment in a given region and the use of such equipment. The strongest predictor of catheterization in a study of acute myocardial infarction was the availability of onsite angiographic facilities (8). Other studies have confirmed this relationship across a variety of health care practice settings. More recent studies have demonstrated similar correlations between the availability and use of nuclear equipment in a given area and the additional correlation between rates of cardiac catheterization and coronary revascularization (9). These data suggest that the use of non-invasive diagnostic technologies appears to have a multiplying effect on subsequent cardiac resource utilization.

The important question raised by these studies of the variation in cardiac procedure utilization is which rate is

“right.” Specifically, is higher use in a given region or among those cared for by sub-specialists indicative of “over-use” of procedures or is there “under-use” elsewhere? The available literature on this topic is conflicting. Various studies have examined the appropriateness of cardiac procedures in various settings. In the majority of these studies, even in high-use areas, more patients with accepted indications for a procedure (ACC/AHA Guidelines, Class I Recommendations) do not receive the procedure compared with those patients who receive procedures without an accepted indication or with a contraindication (ACC/AHA Guidelines, Class III Recommendations) (11). Studies examining the impact of this variation in care on patient outcomes have had conflicting results. Some studies show that patients treated in regions with lower utilization of invasive procedures have outcomes similar to those treated in regions using more resource-intensive care strategies (6,12,13). Other studies, however, have found that patients treated in regions using more invasive procedures had fewer symptoms and improved long-term survival (14). Outcomes in acute myocardial infarction are better when the admitting physician is a cardiovascular specialist, reflecting higher usage of appropriate medications and procedures (15).

ENSURING APPROPRIATE USE OF PROCEDURES

Various options exist for managing potential conflicts of interest regarding self-referral in clinical practice. In-office/in-lab procedures performed in accordance with ACC/AHA guidelines by a physician who is competent in the performance of the procedure simply reflects efficiency and the appropriate standard of care. Physician ownership of medical equipment, especially high-cost, high-revenue

equipment, is a complex professional issue. In all cases, the ownership should be fully disclosed to the patient as described in the American Medical Association (AMA) Code of Medical Ethics (16). The core question is whether clinical decisions are in the patient's interest or influenced by potential personal gain by the physician owner. Although this potential conflict exists, these arrangements may improve access and quality of care for patients. In general, the following approaches should optimize care and reduce concerns about inappropriate self-referral:

- use of evidence-based guidelines
- physician and laboratory credentialing
- periodic case conferences
- oversight/review processes
- consultation with other providers
- full discussion with the patient regarding risks, benefit, alternatives, and the option for a second opinion
- disclosure/transparency of ownership

Utilization of ACC/AHA practice guidelines and clinical competence statements. The cardiovascular community has access to extensive and disease-specific treatment guidelines to inform diagnosis and treatment decisions. These joint ACC/AHA documents include comprehensive guidelines for the management of most major cardiovascular diseases, including acute coronary syndromes, stable coronary artery disease, congestive heart failure, valvular heart disease, atrial fibrillation, supraventricular arrhythmias, and preoperative evaluation for noncardiac surgery. Additional guidelines for specific therapeutic interventions are available including percutaneous coronary intervention and coronary artery bypass surgery. Utilization guidelines for most technical procedures have been developed by the ACCF, the AHA, and other subspecialty societies. These include guidelines for echocardiography, electrocardiography, ambulatory electrocardiographic monitoring, cardiac catheterization, nuclear studies, pacemaker-implantation, and exercise testing.

Where appropriate, guideline-writing groups include representatives from many specialties, including cardiovascular surgery, internal medicine, family practice, emergency medicine, and anesthesiology. These guidelines are easily accessed, either in full text or in an executive summary form on both the ACCF and the AHA web sites (www.acc.org and www.americanheart.org) and can be downloaded to handheld computers. The guidelines are reviewed at least yearly and updated as needed. Thus, current evidence-based information about best practices is now available to physician, payer, and patient alike, providing a powerful resource for appropriate evidence-based care (17,18). These guidelines also provide recommendations for the frequency of performance of office procedures and allow responsible parties to play a key role in understanding the need for testing. Specific recommendations for the performance of diagnostic and therapeutic interventions are thus clearly defined and are available to the entire health care commu-

nity; these broaden participation in determining when and in whom to carry out patient interventions.

The ACC/AHA guidelines form the basis for three additional instruments of great value in providing continuous quality improvement. Systems-based approaches such as the ACCF's "Guidelines Applied in Practice" and the AHA's "Get With the Guidelines" programs have been shown to enhance effective application and improve outcomes (19). In addition, performance measurements are being developed jointly by the ACCF and the AHA for performance improvement and appropriateness of care. Closely related are issues of physician training and competence in performing specific procedures. Practitioners performing procedures on their own patients or by referral should achieve certification of adequate training and maintenance of competence over time. The ACCF, the AHA, the American Board of Internal Medicine, and subspecialty groups have developed a series of documents that detail the appropriate training and experience for competence in a wide variety of cardiovascular procedures (20).

Laboratory oversight. Appropriate oversight by physician laboratory directors is another approach to monitoring self-referral while broadening responsibility and encouraging proficiency in the performance of procedures. Regular review by physician directors of catheterization, echocardiography, nuclear, and other laboratories is important in ascertaining that indications for patient referral, procedural quality, and outcomes all are satisfactory. Additionally, they ensure that caseload or other factors do not drive clinically inappropriate laboratory utilization.

Participation in laboratory databases is essential, with regular review and comparison to databases such as the ACC National Cardiovascular Data Registry™ (21), which can be used for benchmarking of individuals, groups, or hospitals. While it is often difficult to determine the appropriateness of any single procedure in any single patient, patterns of "diagnostic yield" from these tests can be helpful. For example, a laboratory whose rate of finding non-occlusive coronary disease that is significantly higher than one's peers may need to review its selection criteria and threshold for testing. Professional review groups consisting of experts from outside of the geographic region also can be employed when local review is impractical. Diagnostic laboratories should participate in accreditation and credentialing.

Broadening health care responsibility. Given that the potential for real or unconscious bias can be driven by financial conflicts, another approach to avoiding such bias is to involve other physicians without any financial stakes in either clinical case-management conferences or conjoint patient management.

Although the vast majority of care decisions are made on an individual physician-patient basis, the potential for inappropriate self-referral may be moderated by employing clinical case conferences. Such meetings may include invasive and non-invasive cardiologists, primary care providers,

independent cardiovascular surgeons, cardiac care associates, and others, thus broadening the input into patient management decisions.

Another approach for responsibility sharing involves “partnerships in care,” wherein patients are cared for jointly by their primary care provider and a cardiovascular specialist. In this care model, it is implicit that the cardiologist will perform specialized diagnostic and therapeutic procedures, with input from the referring and consulting physician, as well as from the informed patient.

Physicians are often viewed by their patients as having ultimate authority in health care decisions. Therefore, physicians must present the patient with a comprehensive discussion of treatment alternatives, including the option to do nothing, along with the relative risks and benefits of each alternative course. Whenever doubt exists on the part of the patient or the physician, there should be the opportunity to seek additional opinions. For example, patients proposed for multivessel angioplasty should generally be told of surgery as an alternative and have the opportunity to consult a cardiovascular surgeon. For those patients who cannot or will not participate in a discussion of care alternatives, it may be appropriate to involve other family members, friends, spiritual advisors, and patient advocates in decision making. In summary:

- The ACC/AHA guidelines are available for most cardiovascular conditions and for diagnostic and therapeutic procedures, and are readily accessible to physicians and patients on the ACC and the AHA web sites.
- Physician compliance with ACC/AHA guidelines for management of patients with cardiovascular disease represents appropriate care in the majority of cases, and such compliance should reduce concerns about self-referral by cardiovascular practitioners.
- Procedural oversight by a professional laboratory director and laboratory accreditation are both essential.
- Both procedural training and the credentialing of physicians, technicians, and other health care providers are critical to good care.
- Involving other health care providers in medical care decisions, such as cardiovascular surgeons and primary care providers, limits bias.

DIRECT-TO-CONSUMER ADVERTISING AND SCREENING

Advertising of health-related services and products has grown significantly in recent years. Direct-to-consumer (DTC) advertising appears to be well entrenched and has been legal for pharmaceuticals since the early 1970s. More recently, advertising in the public media has grown rapidly for medical devices, diagnostic testing (such as computed tomography-based coronary artery calcium screening or cholesterol screening), and for many non-cardiac or related procedures. Sometimes performed in shopping malls or church parking lots, these activities have raised a variety of

ethical concerns for the medical profession. At question is the propriety of such DTC advertising, physician ownership or investment in such enterprises, concern about patient referral by a physician to a facility in which he or she is an owner or investor, and the value of such screening in promoting the public health.

Physician advertising is now recognized as legal under the provisions of Section 5 of the Federal Trade Commission Act. Regulations were clarified extensively by the Food and Drug Administration (FDA) in 1997, including such language as the requirement for “adequate provision: side effects, contraindications, and effectiveness—this should include either reference to a toll-free phone number, a referral to a physician or pharmacist, a referral to a print advertisement containing a summary of risk, and a web site.” No such guidelines exist for device manufacturers for diagnostic testing; in fact, the FDA has opposed some of the diagnostic screening and testing advertisements (22,23).

Both the AMA and the American College of Physicians have reviewed these issues and published similar guidelines (4,5). These guidelines state that such advertisements “shall not be misleading because of the omission of necessary material information, shall not contain any false or misleading statement, or shall not otherwise operate to deceive.” The AMA states that advertisements should “communicate the information contained therein to the public in a readily comprehensible manner” (22,23). Further, “the key issue, however, is whether advertising or publicity regardless of format or content is true and not materially misleading.” It thus seems clear that advertising per se is professionally accepted and legal, and the issues are those of appropriate content and disclosure.

Guidelines similar to those for DTC pharmaceutical advertisements seem appropriate and in part have been proposed by the AMA for DTC advertising of diagnostic testing. Where cardiovascular testing is involved, professional societies such as the ACCF and the AHA should assume a leadership role in defining these guidelines at the policy level rather than at an individual patient level. In summary:

- The DTC advertising for diagnostic tests is unregulated and needs oversight by appropriate regulatory agencies.
- Professional societies should develop guidelines for such advertising and for the appropriateness of such tests.

CARDIOVASCULAR SPECIALTY HOSPITALS AND SELF-REFERRAL

The role and quality of specialty hospitals. Cardiovascular specialty hospitals are a recent phenomenon. Although cardiovascular care has traditionally been a component of full-service general hospitals, in recent years a small number of free-standing cardiovascular specialty hospitals have been created. Virtually all of these hospitals are for-profit and are located in jurisdictions with minimal or absent governmental control over the creation of health care facilities.

The cardiovascular specialty hospital vision is a facility specifically tailored to provide optimal cardiovascular care. Ideally, a dedicated heart hospital can operate without any of the compromises that result from the design and resource competition issues of a full-service hospital. Such facilities typically offer complete inpatient and outpatient cardiovascular diagnostic and therapeutic services, but often do not provide many of the non-cardiovascular services that are traditionally included in a full-service hospital. Several incentives foster the creation and operation of heart hospitals:

1. The heart hospital architecture, equipment, and operational protocols can be optimized for cardiovascular care. Thus, it has the potential to provide the best working environment for cardiovascular health care providers and an optimal clinical care environment for patients.
2. Reimbursement rates for cardiovascular care under prospective payment systems are generally favorable. This gives the heart hospital reasonable reimbursement and a greater potential to be profitable, when compared to the full-service hospital, which provides many services for which prospective payment is less favorable.
3. Full-service hospitals, unlike heart hospitals, may divert revenue from cardiovascular care to support other service lines that are less well reimbursed. This does not happen in a heart hospital.

Conversely, there are potential concerns about the appropriateness and positioning of such institutions in the overall health care system. For example:

1. Can such institutions provide optimal care to all cardiovascular patients?
2. Do such hospitals undermine the strength and integrity of full-service hospitals?
3. Do physicians who invest in these for-profit hospitals have a conflict of interest when deciding where to admit a particular patient?

The U.S. General Accounting Office recently released a study of specialty hospitals in the U.S. that was commissioned by the U.S. Congress (24). It identified 15 currently operating heart hospitals with approximately a dozen more in various stages of planning and construction. Virtually all were for-profit institutions and virtually all had significant investment on the part of physicians who held privileges at that hospital.

With respect to economics and regional competition, the study found that, whereas the majority of heart hospitals were relatively small institutions, generally with 60 or fewer beds, they frequently had a major regional impact in that they tended to deliver a large fraction of the cardiovascular services in their service area. Thus, they had a potentially large impact on the cardiovascular service lines of the competitive full-service institutions in their region. The specialty hospitals tended to have a somewhat more favorable payer mix (smaller fraction of Medicaid-reimbursed

patients) than the full-service hospitals. In addition, specialty hospitals tended to have a slightly lower case-severity index than full-service hospitals. All of these trends work to enhance such institutions' financial performance relative to full-service hospitals.

With respect to clinical quality, other published studies indicate that heart hospitals achieve outcomes comparable to those of full-service hospitals with a potentially reduced length of stay (25).

Ethical issues related to specialty hospitals. PHYSICIAN FINANCIAL CONFLICT OF INTEREST. Most heart hospitals are for-profit. Many are capitalized in part through physician investment. Thus, some physicians who have privileges at a heart hospital have a financial stake in the institution. It has been pointed out that, in most cases, physicians provide less than 50% of the start-up capital and, in general, individual physicians have small ownership shares (26). Thus, it can be argued that an individual physician's financial stake in an institution is modest, and a physician's income is not significantly influenced by the heart hospital's financial performance. However, the physician's capital is at risk, and should the hospital fail financially, he or she would stand to lose the capital investment. Thus, such a conflict might cause a physician to admit less complicated, better insured patients to the heart hospital while diverting the more complex, less well insured patients to the full-service hospital.

IMPACT ON COMPETING FULL-SERVICE HOSPITALS. The full-service hospital is often a vital community resource, and the quality of health care within the community may be dependent upon its financial and clinical success. Heart hospitals can have a competitive advantage over full-service hospitals for several reasons, including more favorable payer mix and the ability to avoid caring for the more complicated cases under the rationale that such patients require services that might be offered only at full-service hospitals. Thus, there is the potential for heart hospitals to "skim the cream" of the cardiovascular service line. At this time, sufficient published studies are not available to evaluate this concern properly. In summary:

- Heart hospitals present an alternative to traditional full-service hospitals for the delivery of straightforward cardiovascular care.
- Heart hospitals have several characteristics that may be appealing to individual cardiologists and their patients.
- Heart hospitals may present a possible conflict of interest for involved physicians.
- Heart hospitals have the potential to affect a community's overall health care delivery system.

The ACC Board of Trustees has not taken a position for or against such hospitals, but has endorsed the following statement: "Given the wide range of opinions expressed by ACC members and the ACC Board of Trustees, the ACC recommends monitoring the data being collected during the

18-month congressionally mandated moratorium on specialty hospitals. There remains significant, unanswered questions about the financial impact on general, acute-care hospitals, patient severity of illness at referral, and quality of care in specialty hospitals. The primary concern of the ACC is delivery of high-quality cardiovascular care to all Americans; sufficient data do not now exist to judge whether specialty heart hospitals are a useful innovation or are detrimental to this mission. The ACC urges use of standardized databases such as NCDR and the Society for Thoracic Surgery in an objective analysis of the performance of specialty hospitals” (ACC Board of Trustees Minutes, December 18, 2003). Likewise, the AHA’s primary mission is the reduction of disability and death from cardiovascular disease and stroke, and in the absence of adequate data, the AHA has not taken a position on heart hospitals. The AHA agrees that the data from the 18-month mandated moratorium must be studied carefully before conclusions can be reached.

LEGAL ISSUES IN SELF-REFERRAL

The anti-kickback statute. Fraud and abuse laws provide criminal penalties to those who knowingly and willfully offer, pay, solicit, or receive remuneration in exchange for referrals of patients or business reimbursed by a federal health care program (27,28). The law was aimed to prevent outright payments for referrals by clinical laboratories, home health agencies, durable medical equipment vendors, and other suppliers. These policies were enacted to:

1. prevent referrals based on financial benefit to the health care provider making the referral, rather than the greatest benefit for the beneficiary;
2. prohibit solicitation of such payments;
3. prevent overutilization of services; and
4. control governmental cost of providing health care coverage.

Violation of the statute is a felony punishable by fines of up to \$25,000 and imprisonment for up to five years. Individuals found guilty might be excluded from participation in federal and state health care programs.

Congress also directed the Secretary of Health and Human Services to develop regulations that would specifically exclude certain arrangements from being considered anti-kickback violations. The safe-harbor exceptions recognize that there are legitimate reasons for a health care entity to pay a physician—as, for example, a hospital medical director—or for clinical laboratory oversight. Potentially illegal hospital-physician incentives have also been defined and can include the use of discounted office space or equipment in facilities usually located near the hospital. Such arrangements are considered inurements designed to influence physicians’ utilization decisions. Fair-market lease agreements are advised to avoid such liabilities. The Office of the Inspector General accepts requests for formal advi-

sory opinions although these may not be relied upon by third parties as legal precedent (28).

The Stark laws. The Stark Law seeks to prohibit referrals by physicians of Medicare or Medicaid patients to facilities in which the physician has an ownership interest or from which the physician receives compensation (28,29). Compensation can be any form of remuneration, direct or indirect, between the physician or family member and the designated health service provider. These include clinical laboratory services, radiology diagnostic services, inpatient and outpatient hospital services, and durable medical equipment covered in the Medicare fee schedule. The Stark legislation is based on the presumption that physicians will overutilize such services if they profit from the referrals or the orders. “Stark” is distinct from the anti-kickback statute. First, Stark evaluates exclusively the financial incentives of the provider making the referral and not the intent of the parties. Second, Stark is a civil, rather than criminal, statute. Violators are not subject to criminal prosecution but may be excluded from federal health care programs and face civil monetary fines.

Much confusion has resulted from the passage of two Stark bills, from the complexity of the laws, and from the slow issuance of rational implementing regulations. Although the basic prohibition for a referral was clearly defined, Stark II provides exceptions to the general prohibition on referrals (29). The most common exception is the in-office ancillary services exception, when the service is performed within a group practice. In summary:

- The Stark law and the anti-kickback legislation are extremely complex and confusing. It has taken 10 years for the government to publish only a portion of the final regulations.
- Safe-harbors are difficult to interpret without legal counsel.
- Although these laws have prevented some of the most ethically egregious examples of kickbacks and fee splitting, they have not limited the significant growth in cardiovascular activities that are in part due to self-referral within the solo or group practice setting.

OVERVIEW AND SUMMARY

Both the ACCF and the AHA take seriously the responsibility of their members to optimize care for their patients. This can best be done by effective application of evidence-based medicine and practicing the highest standards of medical care. The issue of “self-referral” and its possible incentive for inappropriate utilization is an important consideration in medical practice. In this document, we have discussed the pertinent background of this issue and made positive recommendations to address this concern. Most self-referral is entirely appropriate. This “self-referral” is open and obvious to all parties. The management of self-referral also includes procedural laboratory oversight and accreditation and physician competence in a given

procedure. Physician ownership of equipment outside of the physician's practice setting is a complex professional issue and should conform to AMA guidelines, which prominently include full disclosure and transparency.

The commercialization of screening tests and advertisements for these tests are largely unregulated. This field needs both regulatory oversight and guidance from professional organizations such as the ACCF, the AHA, and cardiovascular specialty societies.

Cardiovascular specialty hospitals have raised issues about potential conflicts of interest among physician investors and their possible impact on community hospitals. The ACCF and the AHA have not taken a specific position on this issue, but members of this Consensus Conference currently support the collection of more data about the quality of care and outcomes provided by such hospitals.

Acknowledgments

The authors appreciate the review and commentary provided by J. Ward Kennedy, MD, MACC, FAHA, and Nathan R. Every, MD, MPH, FACC.

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Task Force 5: Expert Testimony and Opinions

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INTRODUCTION

The American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA), premier organizations in cardiovascular medicine, are considered trusted sources of consensus about matters related to cardiovascular health. It is important to make clear when one is or is not representing one of these organizations.

HOW DOES ONE DIFFERENTIATE AND DESIGNATE PERSONAL PROFESSIONAL OPINION FROM EXPRESSION OF THE POSITION OF THE ACCF OR THE AHA?

Members of the ACCF or the AHA have a variety of roles aside from their professional relationships with these organizations. Delineation of these varying roles may not always be entirely clear. A member's particular expertise in research or as a care provider naturally provides the impetus for his or her official contributions to the organization's programs, written position statements, and guidelines. Individuals may also serve each organization in a variety of official capacities, including as officers, board members, committee chairs, and members.

It is the responsibility of the individual member not to misrepresent or imply an opinion as being that of the ACCF or the AHA unless the person is functioning as an officially designated representative of either organization. This may require a formal statement by the individual to exclude any possibility that his or her personal opinion could be reasonably interpreted as being that of the organization (as may be the case if one's organizational service or contributions are highlighted as part of one's qualifications as an expert), unless organizational affiliation is absent from the stated qualifications. This is particularly important if the expert is an officer, board member, or committee chair of the ACCF or the AHA.

HOW SHOULD THE ACCF AND THE AHA DESIGNATE A SPOKESPERSON FOR A SPECIFIC ISSUE?

An individual's qualifications as an expert are often based on recognized clinical expertise, which is at times difficult to quantify, or on one's contributions to medical knowledge based on research productivity as reflected in peer-review publications. Both ACCF and AHA volunteers (and staff)

file annual conflict of interest declarations. Spokespersons for specific topic areas should have expertise in that area based on qualifications noted in the preceding text, and, wherever possible, should not have any actual or perceived conflicts of interest that could influence their opinions or call into question the independence or integrity of the organization's positions. If it is not possible to find a spokesperson without such conflicts, these conflicts must be clearly stated.

WHAT ARE THE RESPONSIBILITIES OF INDIVIDUAL MEMBERS ACTING AS EXPERT WITNESSES IN LITIGATION REGARDING INDUSTRY?

The ACCF supports the concept that the cardiovascular specialist has the obligation and duty as a citizen, a physician, and a member of a profession to act as an expert witness in litigation where issues appropriate to his or her training and expertise are involved to see that justice is done to both the plaintiff and the defendant. Undeniably, it is true that physicians may be wrongly accused of malpractice when a bad outcome not due to negligence has occurred. It is also true that physicians have injured patients as a result of negligence or malpractice. The interests of society and the medical profession are best served when scientific and unbiased expert witness testimony is available to both plaintiffs and defendants in medical malpractice litigation. Acting as an expert witness, the physician serves as a knowledgeable, experienced, impartial individual, presenting his or her own considered opinions of the case and not acting in any official ACCF capacity.

Suggestions to encourage physicians to act as expert witnesses and discourage the use of "professional expert witnesses" have been offered, each of which has merit. One suggestion is that medical schools include training of physicians in the skills required to act as an expert witness (1,2). Another suggestion is that the medical societies maintain a list of qualified physicians willing to act as expert witnesses so that the lawyers can use this as a pool of medical experts from which to draw (3,4).

The American Medical Association has written that medical expert witness testimony is effectively part of the practice of medicine (5). The expert witness either for the plaintiff or the defendant is not an advocate for the side that has engaged him or her; that is the duty of the lawyers. Before agreeing to act as an expert witness, the physician should assess the merits of the case and give an honest

opinion to the requesting attorney (6). The role of the expert witness is to assist the judge and jury to understand the medical facts of the case. As such, the expert witness acts both as a consultant to the court and as a teacher (7,8). The testimony must be honest, objective, and fully impartial regarding the medical information in the case. Because judge, lawyers, and jury are lay people, the medical testimony must be clearly stated, concise, and understandable. The expert witness should review all of the relevant records used to establish the facts of the case as well as the standard of practice as it existed at the time of the alleged occurrence. The expert witness has the ethical obligation to give truthful answers within the bounds of his or her expertise and must be able to sincerely and validly justify the position he or she believes. Consequently, physicians acting as expert witnesses should be willing to testify for plaintiffs or defendants in different cases depending on the merits of the case. Proper expert testimony is balanced, and where doubt exists, such doubt should be readily admitted (9).

In 1990, the Guidelines for the Physician Expert Witness were published by the American College of Physicians (ACP) (10). On October 15, 1995, the ACC Board of Trustees approved this policy statement, which is derived from the ACP guidelines (11).

Medicine, as a profession, has the obligation to police itself (3). Poor practitioners who are a danger to their patients should be held accountable, and good physicians mistakenly accused must be defended (9). The expert witness testifying to the standard of care should be of the specialty or field that is the same as the defendant physician or medical professional. An internist or family-practice physician should not be held to the same standard of care as a cardiologist. Within the field of cardiovascular disease, a general cardiologist can act as an expert witness in all aspects of the diagnosis and general management of patients with cardiovascular disease. Questions involving technical details of an interventional or electrophysiologic procedure should be the province of a practicing specialist who is board certified in these areas.

RECOMMENDED CRITERIA FOR EXPERT WITNESSES IN MALPRACTICE LITIGATION

1. The cardiovascular expert witness must have a current, valid, and unrestricted license within his or her area of professional practice.
2. For medical testimony in the field of cardiovascular disease, the expert witness should be board certified by the American Board of Internal Medicine or the American Board of Osteopathic Internal Medicine in the specialty of cardiovascular disease or equivalency in pediatric cardiology or cardiovascular surgery. The cardiovascular expert should be actively and primarily engaged in the practice of the specialty or subspecialty under consideration. Similar criteria apply to the cardiovascular subspecialties, such as electrophysiology and interventional cardiology.
3. For testimony by other health care professional expert witnesses, the experts should have equivalent qualifications appropriate to their area of practice.
4. The expert must be knowledgeable, familiar with, and qualified in the specific area in which he or she is testifying, and with commonly accepted clinical practice standards as they relate to the case and locale.
5. Compensation for expert testimony should be reasonable and commensurate with the time and effort expended. It is unethical for an expert witness to accept compensation that is contingent on the outcome of litigation.
6. The expert witness should be willing to submit transcripts of prior and current depositions and courtroom testimony for peer review.
7. Expert witness testimony should be fair, thorough, and objective. It should not exclude any relevant information that has a bearing on the case.

WHAT ARE THE RESPONSIBILITIES AND/OR OBLIGATIONS OF INDIVIDUAL MEMBERS ACTING AS EXPERT WITNESSES IN OTHER LITIGATION, CLASS ACTION LITIGATION, OR PATENT ISSUES, REGARDING THE PHARMACEUTICAL AND MEDICAL DEVICE INDUSTRIES?

The expert witness should testify in the area of his or her expertise. Unfortunately, not all expert witnessing is done by experts (12). There are physicians who have become "professional expert witnesses" or "hired guns" and make their entire living testifying as "medical experts" (3). Their testimony may not always be objective and unbiased, and they may function as partisans rather than scholars (1,8). They exist because physicians have been reluctant to testify as expert witnesses for several reasons: distrust of lawyers, uneasiness with the legal system and the process of testifying, not wanting to encourage malpractice or other types of lawsuits, and fear of being censured by other physicians (13). The AMA, the ACP, and the ACCF have all made strong recommendations that it is the duty of physicians to act as expert witnesses in their areas of expertise (9,11,14). With the availability of adequate numbers of physicians willing to act as expert witnesses, it is hoped that the use of the "professional expert witness" will decrease (10).

Expert witnesses must be truthful, and violators should be sanctioned. The question remains as to what mechanism should exist to perform the necessary function of developing disciplinary steps to deal with the physician who gives false expert witness testimony. Numerous suggestions have been made (12). Among these is that the ACCF should have a panel to review cases where physicians have been accused of giving false or misleading expert testimony, as has been done by other organizations (i.e., American Academy of Neurology) (12). It is possible that this could lead to

controversy among the Fellows of the ACCF and litigation against the organization and could entail significant investment of time and money. The issue is an important one and requires additional discussion to determine the best approach. If such a panel is created, it is suggested that the review of cases be narrowly focused on the contested testimony of the expert witness. Another suggestion is to include independent court-appointed, expert filing of opinion letters by experts with supporting documentation, and a sanction process by courts and/or authoritative boards for testimony that is deemed inaccurate, false, or contradictory to the standard of care (15). This, too, requires further discussion.

In product liability litigation, class action litigation, and patent issues regarding the pharmaceutical and medical device industries, court-appointed neutral expert witnesses identified by the appropriate medical societies could play a constructive role in providing unbiased testimony in medical legal disputes. All of the professional and ethical behavior characterizing the conduct of an expert witness should apply.

Experts in the media. When an expert is contacted by the media for an opinion, he or she must make it clear whether the opinions expressed are the individual's personal opinions or whether the expert is acting as a spokesperson for the ACCF and/or the AHA. If the latter, the individual must be certain that he or she accurately expresses the position of the organization.

Experts providing public testimony. When an expert is asked to testify before Congress or another government body, a different level of responsibility exists. If the expert is acting only as a witness in the area of his or her expertise and not representing an official position of the ACCF and/or the AHA, then the expert should clarify that he or she is expressing a personal/professional opinion. However, if the expert is testifying about the position of the ACCF and/or the AHA, then this testimony carries the weight of the community that is represented by the ACCF and/or the AHA. Such a witness either should be appointed by the organization to represent its official position, or he or she

should make clear that the views expressed do not represent the organization.

When an expert witness is testifying about what is said in an ACC/AHA guideline, if what he or she quotes is directly from the guideline, then that has the imprimatur of the ACCF and the AHA. It makes no difference whether the physician was or was not on the writing committee for that guideline. It is what is in the guideline that has the official endorsement of the ACCF and the AHA.

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Task Force 6: Code of Conduct for Staff and Volunteer Leadership

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INTRODUCTION

Over the past several years leadership in general, and corporate leadership in particular, has come under warranted scrutiny by the American public not only for unethical but, in many instances, fraudulent practices. The professions, and particularly the medical and scientific professions, have also been placed under increased scrutiny by government officials and the public. To be sure, these stains on the moral fabric of American leadership are spotty and hardly reflect the norm that characterizes the leadership of the totality of American enterprise. Notwithstanding, it seems both timely and important to examine and codify, if possible, the behavioral patterns that should be operative within the leadership of organized cardiology as reflected in its two principal institutions, the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA). The goal of this Task Force is to highlight those high moral and ethical standards that will serve to convey the integrity and professionalism of our organizations. It is the obligation of leadership and staff to reflect values by acting in a morally responsible and professional manner.

The ACCF and the AHA are both uniquely intertwined with the dual obligation that the health care professional (HCP) has to both the patient and to society. The primary obligation of the HCP is to the patient and to do that which is best for his or her well-being. This is the principle of *beneficence* (the obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm). In addition to supporting members in caring for individual patients, the ACCF and the AHA must also address societal concerns and adhere to the principle of *distributive justice* (which requires that the benefits and burdens of research and other health care resources be distributed fairly). Another tension is the dual obligation of the ACCF and the AHA to advocate for their professional members, and to advocate for patients and society as a whole. These multiple responsibilities, with their inherent tensions, mandate that the basic tenets of organized cardiology must be founded on a moral model in addition to the economic and contractual models currently practiced throughout corporate America today. This premise was set forth almost 15 years ago in 21st Bethesda Conference:

Ethics in Cardiovascular Medicine (1), and what holds true for the contemporary HCP most certainly applies to its corporate leadership. The face of American cardiology is reflected in the image of both the staff and the volunteer leadership of the ACCF and the AHA as seen not just by patients but also by the scientific and clinical communities, the public-at-large, the media, government, industry, and corporate America. Additionally, the ACCF's and the AHA's tax-exempt status carries further obligations to society. Accordingly, in this Task Force report we have attempted to underscore those qualities essential to the structural and operational prerequisites that constitute the moral model. This is as difficult as it is similar to the Aristotelian concept of defining the *virtuous man*.

A statement of the problem. Upon reflection, it would appear that over the closing decades of the last century there has been an erosion of trust pervasive throughout this country in virtually all sectors of society. The hyperbole associated with current marketing techniques, the expanded media coverage with its emphasis on sensationalism, and a generally fading "truth-in-lending" ethos are likely contributing to the erosion of what used to be a solid and generalized trust. More subtle forces probably explain other acknowledged ills we witness today, which range from grade inflation to an absence of accurate disclosure in letters of recommendation, from failure of full disclosure to false claims, and from overpricing to outright stealing, to identify but a few. Mistrust has tainted such icons as the New York Stock Exchange and many of its leading members, the Olympic Organizing Committee, the Federal Bureau of Investigation laboratories, prominent philanthropies, and even to the churches of organized religions. The professions of law and medicine have also been caught in the glare of this penetrating spotlight. Only recently, cardiology itself had to endure the revelation of alleged greed within a medical institution in California (2). Stories of conflict of interest linked to biased clinical research continue to emerge.

Amidst this threatening climate it seems prudent to examine *integrity* and *trust* as they presently exist within all reaches of cardiovascular medicine. Where they are found lacking or weakened, remedies need to be devised for their restoration. Although this is the overarching objective of the

Consensus Conference, this Task Force addresses the delineation of a code of conduct for staff and volunteers and has identified three separate areas that relate to the issue of *trust in cardiovascular medicine*: 1) the moral obligations of its leadership, 2) the stewardship of the organization, and 3) the identification of potential or perceived conflicts of interest.

These are meant to apply to anyone in a position of authority, influence, or privileged knowledge. It is also meant to apply to conduct governing professional and interpersonal relationships, including staff-to-staff interactions, staff-leadership interactions, staff-volunteer interactions, and volunteer-to-volunteer interactions.

MORAL OBLIGATIONS OF VOLUNTEER LEADERSHIP AND SENIOR STAFF OF NON-PROFIT ORGANIZATIONS

The law generally imposes three primary obligations on the members of the board of a charitable organization (3). The first is a “duty of care,” which means that board members will act with the same degree of care or diligence as they would in their own personal or professional activities. The second is a “duty of loyalty,” which means that a board member must always act in good faith and avoid placing his or her own interests ahead of those of the organization. The third is a “duty of obedience,” which means that a board member must faithfully discharge the obligations imposed on him or her by law and by the corporation’s bylaws and policies. Senior staff and volunteer leadership of a non-profit organization share on a moral level these duties to protect and care for the organization they serve and the resources they steward (4).

These duties obligate senior staff and volunteers to take the time to inform themselves of the organization’s bylaws, policies, and procedures. Only by so doing can senior staff and volunteers ensure that, in carrying out their duties as volunteer leaders or senior staff, they avoid misrepresenting or misstating the organization’s position or taking action in conflict with its established policy or consenting to or participating in inappropriate actions or decisions of others in the organization.

Volunteers and staff should act only within the scope of their authority. For example, in their contact with potential donors, they must avoid making promises they lack the authority to make or that the organization is not capable of filling without violating its established policies and procedures. In contacts with the press, both volunteers and staff must avoid making statements regarding the organization’s position unless the organization in fact has an established position and unless these individuals are authorized and prepared to comment on it. In contact with public officials, both volunteers and staff members must exercise care in lobbying and political activities to avoid jeopardizing the organization’s tax-exempt status or subjecting it to criticism in the press. In general, volunteers and staff must avoid committing the organization to any action unless they are

duly authorized to do so. Creating unfulfilled expectations on the part of donors or other members of the public tends to erode the trust or goodwill on which the organization’s success is based.

Volunteers and staff must always act in accordance with the organization’s policy and should understand and respect the dynamic of governance/policy-setting and distinguish it from operational/management decision-making. Also, volunteers and staff must diligently carry out agreed-upon tasks and assignments, knowing that their failure to discharge undertaken tasks may expose the organization to embarrassment and legal claims, and may jeopardize the organization’s ability to accomplish its mission. This is particularly a risk in the case of volunteers who at the time they agree to do something may fail to recognize the consequences to the rest of the organization of their own failure to perform. Prudent staff and governing bodies recognize this risk and manage their volunteers accordingly.

Volunteers and staff must protect the confidentiality of their organization’s information, such as its intellectual property, its business and operational plans, its personnel information and actions, member lists, and the identity of individual donors.

Moreover, volunteers and staff should understand that the organization’s reputation, which is so important to its ability to accomplish its mission, is based on the public’s trust, which, as recent events make clear, is fragile and can easily be eroded. To protect this public trust, volunteers and staff members should report misconduct by others in the organization to the appropriate officials who have the authority to deal with it.

The ACCF and the AHA, as organizations sensitive to ethical issues, should have a carefully articulated set of core values. All volunteers and staff have a responsibility to adhere to these values, especially senior volunteers and staff, who are obligated to set an example for other staff and volunteers and also to the public.

It is the expectation that, during deliberations, differences of opinion may arise; these differences are encouraged and should be aired. However, once a final decision has been duly made by the organization, members of the board and senior staff should support it.

STEWARDSHIP OF THE ORGANIZATION

It is the duty of the membership, both volunteer and staff, to support and achieve the principal aims of the organizations they serve. The leadership, both volunteer and staff, have the added obligation of assuming the stewardship of their respective organizations. Because this entails not only oversight, management, and, in some instances, fiduciary responsibility, their efforts must also be directed at achieving and ensuring optimal value of their undertakings and decision-making on behalf of the organization.

The organization must have policies and supporting procedures for the following:

Reputation/Integrity

1. Expenditure/use of resources to assure that they are for the organization's benefit, and within the organization's operational plan, not for personal benefit.
2. Purchasing and vendor selection to assure decisions are made on appropriate criteria and with appropriate authorizations.
3. Relationships with industry to assure that both volunteer and staff are sensitive to the issue of conflict of interest and guide them to act in the interest of the organization, not for self or other organizations, and that decisions are not tainted by perceived or real conflicts or personal gain.
4. Nominations/elections that assure qualified candidates are identified and nominated for leadership positions and who have leadership abilities, competencies appropriate to that organization, and high ethics and integrity.
5. Board-operating policies that can address issues related to board members or others requesting resources/actions that are unsupported by board policy, and issues related to unprofessional conduct in board meetings and other leadership meetings.
6. Internal and external controls and audits to protect the financial and accounting integrity of the organization.
7. Internal audit or other process for identifying and addressing non-compliance with policies and procedures.
8. Employment practices/policies including: a) hiring/discipline/firing policies to protect both the rights of candidates/employees and those of the organization; b) grievance process for employees who believe they have been treated unfairly, which requires a response by management and which also protects the employee against retaliation or discipline for making a good-faith grievance; and c) policies to assure proper oversight of compensation practices.
9. Protecting the integrity of the organization's name, logo, assets, and reputation so they are not used for unauthorized purposes or for personal gain, including misrepresentation of the organization's position or misuse of one's employment by or leadership position with the organization in consultation, expert testimony, or personal endorsements.

Legal/Regulatory

1. Compliance with laws including those governing financial reporting, employment and compensation, privacy, fiduciary duties, and not-for-profit obligations and restrictions (e.g., taxes, solicitations, lobbying, political activities, compensation).
2. Process for volunteers and staff to identify suspected violations of policies, laws, or ethics to a designated organization official, which assures anonymity and no retaliation. Also, procedures to address suspected violations that assure fairness to all parties should be in place.

3. Examination of the Sarbanes-Oxley Act (Sarbanes-Oxley Act of 2002; P.L. 107-204) and implementation of those provisions that are relevant and appropriate to the organization, including, at a minimum, provisions to assure independent and financially literate audit committee members, independence and authority of the audit committee to oversee financial reporting and the audit process, and written statements from the chief executive officer and chief financial officer certifying the fair representation of financial information. Although the Sarbanes-Oxley Act applies to public corporations, the law sets standards with which the public will expect private and not-for-profit corporations also to comply.
4. Both a policy and a cultural expectation that volunteers and staff act consistent with and carry out the organization's bylaws/policies.

Authority/Decision-Making

1. Decisions are made according to authority granted and specified in bylaws and policies (e.g., who can authorize what level of expenditures).
2. Decisions carry out the board's policy priorities and intent, and are not based on individual power/influence; and decisions are made in the best interest of the organization as a whole, not of a specific constituency.
3. Board members are provided an orientation, including the board's responsibilities and authorities, the organization's bylaws, policies and strategic plan, applicable not-for-profit laws, and fiduciary duties.

RELATIONSHIPS CREATING POTENTIAL CONFLICTS OF INTEREST

Relationships that can pose potential conflicts of interest exist both internally within the organization and externally. There is potential for conflict on the part of both staff and volunteer leadership. The existence of multiple, overlapping responsibilities and interests can create opportunity for bias, which cannot be addressed unless recognized.

Many kinds of relationships can create a potential for conflict, including, but not limited to, those with industry (e.g., grants, donations, sponsorships, promotions, research funding, consultantships), leadership in other professional societies or consultancies, which may represent either a conflict of interest or a conflict of commitment, obligations to a volunteer's university or employer, relationships with colleagues, family, and household members, and relationships with other businesses or individuals with competing or overlapping interests. Additional potential conflicts may be created by ownership of intellectual property related to the organization's area of expertise or activity, or by investment authority or decision-making responsibility for competing organizations or entities (e.g., other societies, for-profit ventures).

Within these relationships, certain activities/actions are prone to creation of conflict, and they should be viewed

seriously and avoided whenever possible. These center on apparent prospect of gain that could improperly influence judgment and actions, including the actual or apparent possibility of financial, political, or material benefit to self, family, colleagues, or to the organization as a whole. Situations likely to create opportunities for such benefit include possessing the authority for decisions or actions that could possibly interfere with or affect the organization's best interests—including fiscal responsibilities, purchasing decisions, co-ventures with outside entities, and other transactions. Also to be avoided is any situation that has the potential to create an unfair advantage for self, family, and/or colleagues, such as non-merit-based judgment of performance and skills; accepting gifts from vendors; any relationship that results in unfair treatment of employees or volunteers; use of confidential or proprietary information for personal or potential gain, or against the organization's best interests; and agreements with entities for the purpose of receiving favorite status and/or characterized by unethical remuneration (e.g., kickbacks). Requiring particular attention are highly remunerative relationships, such as those with publishers, exhibitors, and high-level supporters. Other mechanisms for the creation of conflicts include misuse of organizational intellectual property, products, or reputation for personal gain or in conflict with the organization's best interests, and whenever demands of outside activities distract from optimal job performance by staff members.

Real or potential conflicts of interest can also be created by industry or other benefactors of the ACCF or the AHA, including staff or volunteers as individuals, offers of research and/or charitable funding accompanied by any actual, apparent, or potential restriction of use of funds or donations that inappropriately accrue to the benefit of donor and are not in the best interests of the recipient (i.e., does not advance the organization's mission). Recognizing the partial financial dependence of the ACCF and the AHA on industry support, situations such as the following should be avoided:

- undue influence, favoritism, or inappropriate recognition of corporate donors,
- soliciting or directing donations to areas of personal gain,
- constraints on publication of research results,
- premature release of scientific or guideline statements,
- activities that involve violation of Accreditation Council for Continuing Medical Education (ACCME) or PHARMA guidelines,
- unrealistic or unethical expectations as to gain, or
- using organizational funds for personal or unauthorized use.

Although intersocietal relationships are beneficial and foster collaboration between organizations, they may also create the potential for conflicts for members or staff who are leaders of more than one related organization, or who

may be perceived as able to disclose confidential or proprietary information.

Because senior officers, selected committee chairs, and journal editors have a unique role in the organizations, the ACCF and the AHA should have well-defined policies regarding relationships that may represent potential or perceived conflicts of interest. These policies should consider which individuals are included and what relationships, if any, may be prohibited.

As avoidance of any real or potential conflict of interest represents an important ethical as well as operational mandate, the ACCF and the AHA should actively recognize the potential problems and develop proactive policies for individuals and the organizations, including codes of conduct, relationships with industry policies that include thresholds for disclosure based on level of financial interest, and disclosure forms and procedures for assessing and ensuring compliance. These should include a definition of conflicts to avoid and statement of principles to follow in staff and volunteer appointments and assignments, regular monitoring of possible sources of conflicts, guidelines for dealing with conflicts (e.g., disclosure, recusing oneself from discussion, non-voting), and procedures for dealing with violations. A component of any policy should include recognition of the obligation of staff and volunteer leadership to set an example by following and promulgating principles of high ethical and moral behavior as well as the obligation of the organization to educate staff, volunteers, and members on these important issues.

Recommendations

1. The organizations should have articulated their core values, which should be supported by a written code of conduct.
2. Board members, staff, and volunteers should act in accordance with their fiduciary, legal, and corporate responsibilities.
3. The organizations should have policies and procedures to protect their reputations/integrity, and to ensure legal and regulatory compliance and proper authority/decision making.
4. The organizations should have conflict-of-interest policies and procedures for both internal and external relationships.

TASK FORCE 6 REFERENCES

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4. Independent Sector. *Obedience to the Unenforceable, Ethics and the Nation's Voluntary and Philanthropic Community*. Washington, DC: Independent Sector, 2002.

Appendix 1. Participants in the ACCF/AHA Consensus Conference on Professionalism and Ethics

Participant Name	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder
Conference Co-Chairs						
Dr. Richard Popp	<ul style="list-style-type: none"> ● Acumen Medical ● Agilent Technologies ● Arnold & Porter ● Bodri Capital Management ● Cardiogenesis Corp. ● Hewlett-Packard Co. ● Advanced Technology Ventures 	None	<ul style="list-style-type: none"> ● Pelikan Technologies ● Point Biomedical Corp. 	None	<ul style="list-style-type: none"> ● Percardia, Inc. ● Sensant Corp. 	<ul style="list-style-type: none"> ● Acumen Medical ● Agilent Technologies ● Hewlett-Packard Co. ● Neoguide Systems ● Pelikan Technologies ● Percardia Inc. ● Point Biomedical Corp. ● Sensant Corp. ● Tissue Link Medical, Inc. ● Zonare, Inc.
Dr. Sidney C. Smith, Jr.	None	<ul style="list-style-type: none"> ● Merck 	None	None	None	<ul style="list-style-type: none"> ● Medtronic ● Johnson & Johnson ● Intuitive Surgical
Keynote Speaker						
Dr. William Parmley	None	None	None	None	None	None
Task Force Co-Chairs						
Dr. Joseph S. Alpert	None	None	None	None	None	None
Dr. Robert O. Bonow	<ul style="list-style-type: none"> ● Bristol-Myers Squibb Imaging ● Takeda ● King Pharmaceuticals 	None	None	None	None	None

Appendix 1. Continued

Participant Name	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder
Dr. Kenneth I. Shine	None	None	None	None	None	None
Dr. Michael J. Wolk	None	None	None	None	None	None
Dr. Douglas P. Zipes	<ul style="list-style-type: none"> ● GMP Companies, Inc. ● Medtronic ● Aderis Pharmaceuticals, Inc. ● Terumo Cardiovascular Systems Corp. ● Life Sentry ● CV Therapeutics ● Burrill and Company ● Genzyme ● Cardiofocus 	<ul style="list-style-type: none"> ● Medtronic 	None	None	None	None
Task Force Writers						
Dr. Robert J. Adams	None	None	None	None	None	None
Dr. Jeffrey L. Anderson	<ul style="list-style-type: none"> ● Merck ● Merck Schering ● Johnson & Johnson/Merck ● Alteon 	<ul style="list-style-type: none"> ● Pfizer ● Novartis 	<ul style="list-style-type: none"> ● Merck ● Johnson & Johnson/Merck 	<ul style="list-style-type: none"> ● Merck ● Bristol-Myers Squibb/Sanofi Partnership ● Merck/Schering ● Pfizer 	<ul style="list-style-type: none"> ● Merck ● Alteon 	None
Dr. Elliott Antman	None	<ul style="list-style-type: none"> ● Aventis ● Bayer ● Biosite ● Boehringer Mannheim ● Bristol-Myers Squibb ● British Biotech ● Centor ● Cor/Millennium ● Corvas ● Dade ● Genentech ● Eli Lilly & Co. ● Merck ● Pfizer ● Sunol 	None	None	None	None
Dr. Bruce Bellande	None	None	None	None	None	None
Dr. George Beller	None	<ul style="list-style-type: none"> ● Bristol-Myers Squibb Imaging 	<ul style="list-style-type: none"> ● Vasomedical 	<ul style="list-style-type: none"> ● Bristol-Myers Squibb Imaging 	None	<ul style="list-style-type: none"> ● Johnson & Johnson ● Pfizer
Dr. Melvin D. Cheitlin	None	None	<ul style="list-style-type: none"> ● Pfizer 	<ul style="list-style-type: none"> ● Pfizer 	None	None

Appendix 1. Continued

Participant Name	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee Stock Holder
Dr. Anthony DeMaria	None	<ul style="list-style-type: none"> All echo instrument and contrast companies 	<ul style="list-style-type: none"> CardioNet Resmed (no salary) 	<ul style="list-style-type: none"> All echo instrument and contrast companies Pfizer 	<ul style="list-style-type: none"> Biosite, Inc.
Dr. Gregg C. Fonarow	<ul style="list-style-type: none"> Merck Pfizer Bristol-Myers Squibb/Sanofi GlaxoSmithKline Astra-Zeneca Guidant Medtronic Scios Schering Plough 	<ul style="list-style-type: none"> Merck Pfizer Bristol-Myers Squibb/Sanofi GlaxoSmithKline Astra-Zeneca Guidant Medtronic Scios 	<ul style="list-style-type: none"> Bristol-Myers Squibb/Sanofi GlaxoSmithKline Guidant Scios Schering Plough 	<ul style="list-style-type: none"> Merck Pfizer Bristol-Myers Squibb/Sanofi GlaxoSmithKline Astra-Zeneca Scios Schering Plough 	<ul style="list-style-type: none"> Bristol-Myers Squibb/Sanofi Astra-Zeneca Medtronic Scios
Dr. Larry B. Goldstein	<ul style="list-style-type: none"> Pfizer-Parke-Davis 	None	<ul style="list-style-type: none"> GlaxoSmithKline CuraGen Corp. DPharm Johnson & Johnson Merck Research Laboratories 	None	<ul style="list-style-type: none"> Pfizer-Parke-Davis None SPARCL Trial
Dr. Augustus O. Grant	None	None	None	None	None
Edward Hines	None	None	<ul style="list-style-type: none"> Investors Financial Services Corp.: NASDAQ Shareholder and Board Member Chase Corp. (AMEX) Board Member 	None	None
Dr. John W. Hirshfeld, Jr.	None	None	None	None	None
Dr. Rae Ellen Kavey	None	None	None	None	None
David Wm. Livingston, Esq.	None	None	None	None	None
Christine W. McEntee	None	None	None	None	None
Dr. Joseph V. Messer	None	None	None	None	None
Dr. Rick A. Nishimura	None	None	None	None	None
Dr. E. Magnus Ohman	None	<ul style="list-style-type: none"> Berkley Schering-Plough Bristol-Myers Squibb Sanofi Millennium 	None	None	<ul style="list-style-type: none"> Medtronic

Appendix 1. Continued

Participant Name	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder
Dr. Robert A. Harrington	<ul style="list-style-type: none"> ● Proctor & Gamble ● Novartis 	<ul style="list-style-type: none"> ● Schering Plough ● Millennium ● Alexion ● Bristol-Myers Squibb ● Aventis ● Eli Lilly & Co. ● Arginox ● Guidant ● Medtronic ● Daiichi ● The Medicines Company ● Astra Zeneca 	None	None	None	None
Marcia J. Jackson	None	None	None	None	None	None
Dr. Harry R. Kimball	None	None	None	None	None	None
Dr. David Korn	None	None	None	None	None	None
Dr. Joao A. C. Lima	None	<ul style="list-style-type: none"> ● Fujisawa ● Toshiba, Inc. ● Merck 	<ul style="list-style-type: none"> ● General Electric Medical Systems ● Amershan 	None	None	None
Dr. Beverly H. Lorell	None	None	None	None	None	<ul style="list-style-type: none"> ● Guidant Corp. (employee & stock holder)
Dr. Jon F. Merz	None	None	<ul style="list-style-type: none"> ● Wyeth 	None	None	None
Dr. Elizabeth Ofili	None	None	<ul style="list-style-type: none"> ● Novartis ● Sanofi 	<ul style="list-style-type: none"> ● Novartis ● Merck & Co. 	<ul style="list-style-type: none"> ● Nitromed 	None
Dr. Carl J. Pepine	<ul style="list-style-type: none"> ● Abbott ● Pfizer ● CV Therapeutics ● Medical Education Consultants, Inc. (MEDCON) 	<ul style="list-style-type: none"> ● King Pharmaceuticals, Inc. ● Monarch Pharmaceuticals ● Abbott ● Berlex Laboratories, Inc. ● Astra Zeneca ● Aventis Pharmaceuticals, Inc. ● CV Therapeutics ● Pfizer ● Wyeth-Ayerst Laboratories 	None	<ul style="list-style-type: none"> ● Medical Education Consultants, Inc. (MEDCON) 	None	None
Dr. Shahbudin H. Rahimtoola	None	None	None	<ul style="list-style-type: none"> ● Pfizer 	None	None

Appendix 1. Continued

Participant Name	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder
Dr. Rose Marie Robertson	None	None	● Merck Pharmaceutical (spouse on SAB)	None	None	None
Dr. Lynn A. Smaha	None	None	None	None	None	None
Dr. L. Samuel Wann	None	None	None	None	None	None
Dr. Gayle R. Whitman	None	None	None	None	None	None

*Educational activities or lectures for this company generate revenue for Duke.